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THE ARCHIVES OF INTERNAL MEDICINE

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CHICAGO
AMERICAN MEDICAL ASSOCIATION
PUBLISHERS

Entered as Second-Class Matter, January 23, 1908, at the Postoffice at Chicago, Illinois, Under Act of Congress of March 3, 1879

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1916

CHICAGO

AMERICAN MEDICAL ASSOCIATION

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CLINICAL CALORIMETRY

NINTH PAPER

FURTHER MEASUREMENTS OF THE SURFACE AREA OF ADULTS AND CHILDREN*

MARGARET SAWYER, B.S.
IOWA CITY, IOWA

RICHARD H. STONE AND EUGENE F. DU BOIS, M.D.
NEW YORK

In paper 5[1] of this series a method was described by means of which it was possible to determine the surface area of living subjects. On the basis of the measurements of five persons of widely varying body shapes, a formula was devised by Mr. Delafield Du Bois which gave an average error of only 1.7 per cent. when applied to the persons measured. The number of subjects was rather small and it has seemed best to continue the work and apply the formula to persons of unusual shapes.

Since the publication of the previous paper, in which the literature was reviewed, a number of references have come to light largely through the attention of Dr. Francis G. Benedict of the Nutrition Laboratory of Boston. The work of Sicheff[2] is of considerable importance. Working in Gundobin's clinic he applied the methods used by Meeh to twenty-four children from the ages of 1 day to 15 years, and to one adult. He found the surface area proportional to the two third power of the weight, but the average constant by which this should be multiplied is 10.7, according to his figures, instead of Meeh's figure of 11.9. In the case of the adult the constant would be 8.8, which is at such variance with the results of other investigators that it would seem as if some error must have crept into the calculations in this one case.

* Submitted for publication Feb. 4, 1916.

* From the Russell Sage Institute of Pathology, in Affiliation with the Second Medical Division of Bellevue Hospital.

1. Paper 5, Clinical Calorimetry, THE ARCHIVES INT. MED., 1915, xv, 868.

2. Sicheff (Ssytscheff), A. I.: Measurement of the Volume and the Surface of the Body of Children According to Age, Inaug. Dissert., Petrograd, 1902. The tables are given in Gundobin, Die Besonderheiten des Kindesalters, Berlin, 1912. We are indebted to Dr. Benedict for permission to consult the translation of the original article in the Nutrition Laboratory.

Variot and Saint Albin[3] have measured the surface of a number of children using pieces of tin foil, and Maurel[4] has worked out the relationship of the thorax dimension to surface area. Letulle and Pompilian[5] in 1906 used a method of determining surface area somewhat similar to the formula adopted by D. Du Bois nine years later. They consider that the surface of the body consists of a number of trapezoids, one covering the upper arm, one the forearm, one the hand, one for each finger, etc. They calculate the area of each trapezoid from the length of the part and the circumference at the two borders which form the sides of the figure. The errors inherent in this method become evident when one looks at the factors used in the "Linear Formula" of D. Du Bois. It is necessary to correct the average length and breadth of each part by a factor to obtain the true surface. Lassabliere[6] measured the surface of a large number of children by marking out the skin in geometrical patterns and determining the area by means of a perimeter. He found the skin area proportional to 10.5 Wt.^{2} or to 0.92 Ht.^{2} or to 2.3 Perim.^{2}, Wt. being the kilograms of body weight, Ht. the height in centimeters and Perim. the circumference of the thorax at the level of the nipples.

INDIVIDUALS MEASURED

Anna M.—This was the cadaver of a child 21 months old, weighed and measured about two hours after death. The subject was small for her age and had suffered from rachitis, the epiphyses at the wrists were large and the thorax was pigeon-breasted, being narrow and very deep anteroposteriorly. The child had pertussis and developed a fatal pneumonia.

Fabian R. S., aged 12 years, 10 months, an unusually well formed boy with no signs of puberty as yet. He was muscular and rather short for his age. He served as the subject for one of the calorimeter experiments described in Paper 12.

Gerald S., 18 years old, tall and much emaciated. He was a diabetes patient and a complete description of his case is to be found in Paper 17. He was given the Allen fasting treatment from November 11 to 19, and the measurements were taken December 1 after he had been on a maintenance diet for about a week. His weight at one time dropped to 38.7 kg., but increased to 45.25 kg. as a result of food ingestion, and also on account of an invisible edema.

ERROR IN PREVIOUS PAPER

A brief preliminary note about the measurements of Gerald S. was given at the end of Paper 5[1] of this series. The discrepancy between the calculated

3. Variot and Saint Albin: La mensuration de l'aitre cutanée des jeunes enfants par l'enveloppement avec des feulles d'etain, Bull. Soc. de pediat. de Paris, 1903, v, 307.

4. Maurel, E.: Adaption de la section thoracique a la surface cutanée par rapport an poids, depuis la maissance jusqu'a l'age adult, Compt. rend. Soc. de biol., 1904, lvi, 980.

5. Letulle and Pompilian: Methode de recherche applicable a l'étude de la nutrition, Rev. Soc. scient. d'hyg. aliment., 1906, iii, 708.

6. Lassabliere, P.: Evaluation de la surface cutanée chez le jenne enfant, Compt rend. Soc. de biol., 1910, 339.

TABLE 1.—Measurements Used in Formula

	Anna M., Cm.	Fabian S., Cm.	Gerald S., Cm.	Emma W., May 3, Cm.	Emma W., May 13 and 17, Cm.	R. H. S. June 18, Cm.	Robert L., Cm.	Harry J., Right Side, Cm.	Harry J., Left Side, Cm.
A Around vertex and chin	49.1	61.5	62.2	64.4	....	67.0	67.9	64.6	....
B Around occiput and forehead	44.0	54.4	51.2	55.0	....	58.0	57.2	55.5	....
F Acromion to lower border of radius	22.9	49.5	65.5	58.6	....	67.7	54.6	59.4	57.7
G Circumference of arm at upper border of axilla	10.5	20.5	20.0	27.5	27.0	26.3	33.6	32.2	34.5
H Largest circumference of forearm	11.9	19.7	21.0	23.4	23.8	25.4	26.2	28.2	29.0
I Smallest circumference of forearm	9.1	13.3	15.0	14.3	14.8	16.7	16.1	16.2	16.5
J—Lower posterior border of radius to tip of second finger	8.7	16.4	19.8	17.5	....	21.9	19.2	17.9	....
K Circumference of hand at knuckles	8.6	17.4	19.9	17.6	....	20 6	20.6	20.2	....
L—Suprasternal notch to upper border of pubes	26.0	46.0	51.3	51.3	. ..	53 6	56.7	50.0	....
M—Circumference of abdomen at umbilicus	35.1	56.8	64.7	71.2	70.1	69.8	92.6	78.2	....
N Circumference of thorax at nipples in male and just above breasts in female	38.6	66.2	78.5	81.0	83.0	85.9	100.6	96.2	....
O Superior border of great trochanter to lower border of patella	16.0	37.8	44.7	45.7	. ..	50.3	47.5	....	....
W Superior border of pubes to lower border of patella	14.4	33.7	44.9	41.7	....	46.3	....	....	....
P—Circumference of thigh at perineum	20.6	41.2	41.4	53.7	55.3	48 3	52.7	....	....
Q—Circumference of hips and buttocks at level of trochanters	39.5	69.7	76.5	93.8	93.2	87 0	94.9	....	....
R Sole of foot to lower border of patella	16.0	36.4	48.3	45.3	....	53.1	....	....	....
S Circumference at lower border of patella	14.2	27.6	31.7	32.0	34.8	34.8	....	....	....
T Length of foot, including great toe	10.5	21.4	26.0	23.3	....	27.5	. . .	....	....
U Circumference at base of little toe	8.9	19.8	21.2	21.3	. . .	21.7	....	....	....
V Smallest circumference of ankle	9.9	16.5	17.8	20.3	. . .	23.8	....	....	....

and measured areas of the thorax was so much greater than in any other case that an error was suspected. It became apparent that the recorded length of the thorax was 10 cm. too short. This measurement L. had been determined by subtracting the distance from foot to upper border of the pubes from III, the distance from foot to suprasternal notch. The recorded measurements in the case of Gerald S. from the sole of the foot were as follows: "To suprasternal notch, 134.5 cm."; to outer end of clavicle, 145.8; to upper border of axilla, 136.2; to tip of ensiform, 125.0; to the nipples, 134.3; height, 171.8. It was evident that the suprasternal notch must have been more than 0.2 cm. above the nipples. To find its correct position the measurements of the five subjects whose shape was nearest to that of Gerald S. were tabulated and the average percentage of the height shared by the distance between suprasternal

TABLE 2.—Measurements Not Used in Formula

	Anna M.	Fabian S.	Gerald S.	Emma W. May 3	R. H. S. June 18
I—Weight, Kg.	6.27	32.74	45.25	57.62	63.00
	Cm.	Cm.	Cm.	Cm.	Cm.
II—Height or length	73.2	141.5	171.8	164.8	184.2
III—Sole of foot to suprasternal notch	54.8	114.7	144.5	135.7	152.2
IV—Sole of foot to nipples	50.4	107.0	134.3	123.9	140.2
V—Sole of foot to upper border of axilla	53.2	109.8	136.2	127.9	145.8
VI—Sole of foot to tip of ensiform	45.6	100.2	125.0	117.5	129.8
VII—Sole of foot to superior border of great trochanter	30.2	73.7	93.0	88.5	103.1
VIII—Sole of foot to perineum	26.6	64.2	86.0	76.4	92.1
IX—Circumference of thorax at tip of ensiform	41.2	65.0	76.5	74.0	78.8
X—Tip of second finger to upper border of axilla	—	.....	67.5	.....	.....
XI—Tip of second finger to tip of olecranon	18.6	37.9	46.9	43.3	51.9
XII—Tip of second finger to metacarpophalangeal joint	4.9	9.8	10.8	10.1	12.3
XIII—Tip of olecranon to lower border of radius	9.8	22.3	28.0	26.0	31.5
XIV—Tip of olecranon to acromion process	13.0	28.0	37.5	32.8	37.7
XV—Circumference of arm at insertion of deltoid	10.4	19.4	18.7	26.0	25.6
XVI—Circumference of arm at belly of biceps	10.6	19.1	18.3	23.8	25.1
XVII—Circumference of thigh half way between anterior superior spine of ilium and lower border of patella	17.8	39.2	37.6	52.2	47.0
XVIII—Largest circumference of calf	13.0	26.6	27.2	35.0	31.0
XIX—Circumference of foot at heel	11.9	26.5	30.2	29.7	31.5
XX—From back of neck around superior maxilla	31.8	42.5	43.5	45.0	48.3
XXI—Around neck just below larynx	17.5	29.0	30.8	33.5	36.5
XXII—Around shoulders at level of heads of humeri	39.8	73.5	87.4	91.0	103.6

notch and various neighboring parts was calculated. The projected location of the suprasternal notch in Gerald's case according to three different methods was 145.6, 142.4 and 144.2. The measurement 144.5 was adopted since it seemed probable that the error had consisted in recording a 3 instead of a 4. Unfortunately the subject had died before the error was suspected and could not be measured again.

Emma W., 26 years old, a sculptor's model. She was well proportioned, slightly above the average height and was neither fat nor thin. She had always been athletic and her muscles were well developed.

R. H. S., 21½ years old. An unusually tall and thin man who had lost about 5 pounds during the past year. For three days before his first measure-

ment an attempt was made to reduce his weight still further. He was kept for two days on a diet low in carbohydrates and salt. On the morning he was measured he took a light breakfast and played tennis for one and one half hours, drinking no water after the exercise.

Robert L., 43 years old. Five years previously he had lost both legs in a railroad accident. The right limb was cut off 50.5 cm. below the superior border of the great trochanter, the left 25.5 cm. below the same point. Both stumps were atrophied from disuse. His face, trunk and arms were fat.

Harry J., 34 years old, colored, usually called "Rubber tires" from the wheels on which he propelled himself with the velocity of a bicycle. His legs had been cut off in a railroad accident when he was only 6 years old. As a result of his deformity he had developed a form which reminded one of a hermit crab. The shoulders and arms were very large and powerful, the hips were those of an undeveloped boy, the stumps were atrophic. The left leg was cut off at the knee, the right about half way up the thigh. Six years previous to examination he had a stroke of apoplexy and the right side of the body was paralyzed, but was now spastic with some power of movement. As a result of this he propelled himself on his wheels and lifted himself about entirely with his left arm, which was unusually strong. He had no superfluous fat on his body.

METHODS USED

The area of the molds was determined by the method of printing on photographic paper and weighing described in Paper 5. In some of the cases, however, the molds were made by new methods, although the paper strip method previously described proved the most accurate and was used in all cases except when specifically noted. The cadaver of the baby, Anna M., was dressed in tight fitting clothing and melted paraffin applied to the whole surface. In the case of Fabian S. the tight fitting underclothing was covered with strips of surgeons' adhesive plaster and over this melted paraffin was painted. This same method was used in the first mold of Emma W. on May 3. It was noted that in both these cases it was comparatively easy to cut the mold open, while with the paper strip method it was hard to get even small probe-pointed scissors between the mold and the skin. This led to the suspicion that the adhesive plaster stretched, so the measurement of four of the parts was repeated with Emma W. Molds of the arm and leg were taken by the paper strip method on May 13, and of the trunk and thigh on May 17, measurements of the parts being made on the same day. The weight on May 3 was 58.09 kg.; on May 13 57.22; on May 17, 57.62 kg. It will be seen in Table 3 that the paper method results were 6.5 per cent. smaller for the arms, 8.6 per cent. smaller for the thighs, 4.5 per cent. smaller for the legs and 1.6 per cent. larger for the trunk. When the totals for the four parts are compared, the paper results are 3.3 per cent. lower, and it may be concluded that the data obtained by the adhesive plaster method in the case of Fabian S. are about 3.3 per cent. too high and therefore should be excluded from the averages.

In all of these subjects the left upper and lower extremities were not included in the molds or in the measurements. In the case of Harry J., molds were made of the trunk and thighs alone, and with Robert L. the mold of the head was omitted.

The measurements were made in the manner described in the previous paper and the same letters and numbers applied to them. In the previous work the measurement F was obtained by adding XIII and XIV, the distance from the tip of the olecranon to the lower border of the radius and from the olecranon to the outer end of the clavicle. These measurements had been made with the arm bent and their sum averages 9.5 per cent. larger than the measurement from acromial process to lower border of the radius with the arm straight. Therefore, in using the formula the measurements should be made with the arm bent or else the factor 0.611 used instead of 0.558.

TABLE 3.—Comparison of Areas of Parts of Body as—

Name	Head			Arms			Hands		
	Measured	Formula	Error, %	Measured	Formula	Error, %	Measured	Formula	Error, %
Anna M.	610	665	+9	486	403	—17	214	166	—23
F. R. S.*	(1037)*	1031	(—0.5)	(1620)*	1478	(— 9)	640	623	— 3
Gerald S.	950	978	+3	2152	2047	— 5	876	875	— 0
Emma W.*	(1079)	1091	(+1)	(2402)*	2132	(—11)	806	683	—15
Emma W.	.....	.....	.....	2252	2145	— 5	...	...	....
R. H. S.	1208	1197	—1	2778	2584	— 7	891	1002	+12
Robert L.	.....	1196	.....	2672	2313	—14	956	878	— 8
Harry J.	.....	1104	.....	.....	2558	.....	...	...	....

* Measured by adhesive plaster method; results average 3.3 per cent. too high.

ACCURACY OF METHOD

In order to give the method of measurement of the surface area a severe test, molds were made of a bowling ball, a perfect sphere with an average diameter of 21.78 cm. and a calculated surface of 0.1490 square meters. The first mold was made by covering the ball with two layers of surgeon's gauze, pasting strips of paper over this, cutting off the mold and coating the inside with paraffin. The area of this mold was found to be 0.1566 square meters, or 5.1 per cent. too large. A second mold was made with greater care. Only one thickness of gauze was used and this was drawn over the ball like a bag, the excess being trimmed off. The paper strips were pasted very tight and the paraffin omitted. The area of the second mold was 0.1488 square meters, or

0.13 per cent. lower than the theoretical surface area. This shows that the method is accurate if the paper be applied very tightly in the manner always used by us, but that if the strips be applied at all loosely, or if a material such as adhesive plaster be used, there may be a plus error of 3 to 5 per cent.

One criticism of the linear formula which has been made is that it would be difficult for two observers to obtain concordant results on the same individual. To test this point a man 182.8 cm. tall, weighing 87.08 kg., was measured by two of the staff independently and the surface calculated according to the "Linear Formula." The first result was 2.0733 square meters, the second 2.0798, the difference being 0.3 per cent. Another subject was measured independently by two physicians, one of whom had never seen the method applied, and the results agreed within 0.5 per cent. This is probably closer agreement

—Actually Measured and as Calculated from Formulas

Trunk			Thighs			Legs			Feet		
Measured	Formula	Error, %	Measured	Formula	Error, %	Measured	Formula	Error, %	Measured	Formula	Error, %
1355	1347	— 1	478	488	+ 2	340	318	— 7	216	205	—5
(4118)*	3978	(— 3)	(2166)*	2130	(— 2)	(1456)*	1407	(— 3)	(834)*	808	(—3)
5003	5165	+ 3	3002	2677	—11	1876	2144	+14	1042	1055	+1
(5526)*	5482	(— 1)	(3608)*	3424	(— 5)	(2392)*	2030	(—15)	(1084)*	1032	(—5)
5618	5522	— 2	3324	3448	+ 4	2288	2207	— 4			
6064	5867	— 3	3155	3457	+ 9	2634	2587	— 2	1251	1301	+4
6897	7701	+12	1755	1781	+ 1						
6599	6130	— 7	794 1196	Right Left							

than would often be found, since measurements of the same part made by one man sometimes differ by 5 per cent. There is no factor except a difference in the tension of the tape which would throw the error in one direction more often than the other.

DISCUSSION OF RESULTS

Tables 1 and 2 give the linear measurements, and Tables 3 and 4 the results of the determinations of the surface area. The individual parts show a somewhat greater divergence between the area as determined by formula and as actually measured than in the former paper, but this was to be expected. The total results are all that could be desired. In the cases of Gerald S. and R. H. S. the errors in the

formula are 0.3 and 0.1 per cent, respectively. With Anna M. and with Emma W. as measured by the paper method, — 2.9 and — 2.0 per cent. The average error for these four subjects is 1.3 per cent. Fabian S. shows an apparent error of 3.5 per cent. when measured by the adhesive plaster method. This would be reduced to — 0.2 per cent if we made the correction for the average plus error of 3.3 per cent. in the adhesive method.

TABLE 4.—SUMMARY

Name	Surface Area		Error, %	Surface Area, Meeh's Formula	Error, %	Correct Constant Meeh's Formula	Age, Yrs.	Weight, Kg.	Height, Cm.
	Measured	Linear Formula							
Anna M.	0.3699	0.3592	—2.9	0.405*	+ 9.3	10.9	2	6.27	73.2
F. R. S.	(1.1869)†	1.1455	(—3.5)	1.260	(+ 6.2)	(11.6)	12	32.74	141.5
Gerald S.	1.4901	1.4941	+0.3	1.563	+ 4.9	11.7	17	45.25	171.8
Emma W.	(1.6897)†	1.5874	(—6.0)	.....	.....	....	26	.....	.....
Emma W.	1.6451	1.6128	—2.0	1.837	+11.6	11.0	26	57.62	164.8
R. H. S.	1.7981	1.7995	+0.1	1.949	+ 8.4	11.4	21	63.00	184.2
Robert L.	1.4299	1.4692	+2.7	1.960	+37.0	....	..	63.81	.....
Harry J.	.....	1.3054	.....	1.800	+38.0	....	..	55.92	.....

* Constant used for Meeh's formula for the baby = 11.9, for adults 12.3.
† Measured by adhesive plaster method; results average 3.3 per cent. too high.

SUMMARY AND CONCLUSIONS

The so-called "Linear Formula" for the estimation of the surface area has been satisfactorily tested on four new subjects of varying size and shape. In addition, partial measurements of two legless men have been made. The average error in the formula when applied to the four subjects was 1.3 per cent. Two of the subjects were children and in these cases the error in the formula was under 3 per cent. Since the youngest was about 2 years old it does not seem advisable to use the formula for babies under this age until the factors have been tested by the measurements of infants.

In conclusion we wish to thank Dr. A. L. Meyer and Mr. G. F. Soderstrom for their aid in making the molds and measuring the subjects.

477 First Avenue.

CLINICAL CALORIMETRY

TENTH PAPER

A FORMULA TO ESTIMATE THE APPROXIMATE SURFACE AREA IF HEIGHT AND WEIGHT BE KNOWN*

DELAFIELD Du BOIS, B.S.
BURLINGTON, VT.
AND
EUGENE F. Du BOIS, M.D.
NEW YORK

Since the publication of Paper 5 of this series the so-called "Linear Formula" has been used in the study of a large number of individuals. Practically all of the subjects of respiration experiments in the Sage calorimeter have been measured in this way, and in addition Means[1] of Boston has used it as a factor in determining his normal base line of metabolism and the extent of the pathological variations. Means has found that the range of normal variation from the average is smaller and that the apparent depression of metabolism in obesity is much less marked when the linear formula, instead of Meeh's formula, is used to determine surface area.

The accuracy of the linear formula has been shown in Paper 9 of this series. In order to correct the slight error in the factor for the arms, and also in order to clear up a few points in the measurements which may cause confusion, it seems best to repeat the formula and show the bony landmarks by diagram (Fig. 1). Some difficulty has been experienced in locating the superior border of the great trochanter in fat subjects. This landmark is the starting point of the measurement "O" which represents the length of the thighs. If we employ another factor we can use the new measurement "W," the distance from lower border of the patella to the upper border of the pubes, a point already located in the measurement "L." In taking this measurement, however, one must be careful to have the legs straight and the knees, heels and great toes touching. It is better to take all measurements from a footboard with the subject lying down,[2] determining distance from soles of feet to lower border of patella, to upper border of

* Submitted for publication Feb. 4, 1916.

* From the Russell Sage Institute of Pathology, in Affiliation with the Second Medical Division of Bellevue Hospital.

1. Means, J. H.: Studies of the Basal Metabolism in Obesity and Pituitary Disease, Jour. Med. Research, 1915, xxxii, 121; Basal Metabolism and Body Surface, Jour. Biol. Chem., 1915, xxi, 263.

2. This is especially important with obsese patients.

pubes, to suprasternal notch and to top of the head.[3] In Table 1 a comparison is made of the old and new formulas for determining the surface of the thighs. It is seen that the average error is the same.

In the literature of the work on respiratory metabolism it has been customary to give only the age, weight and height. If, therefore, we

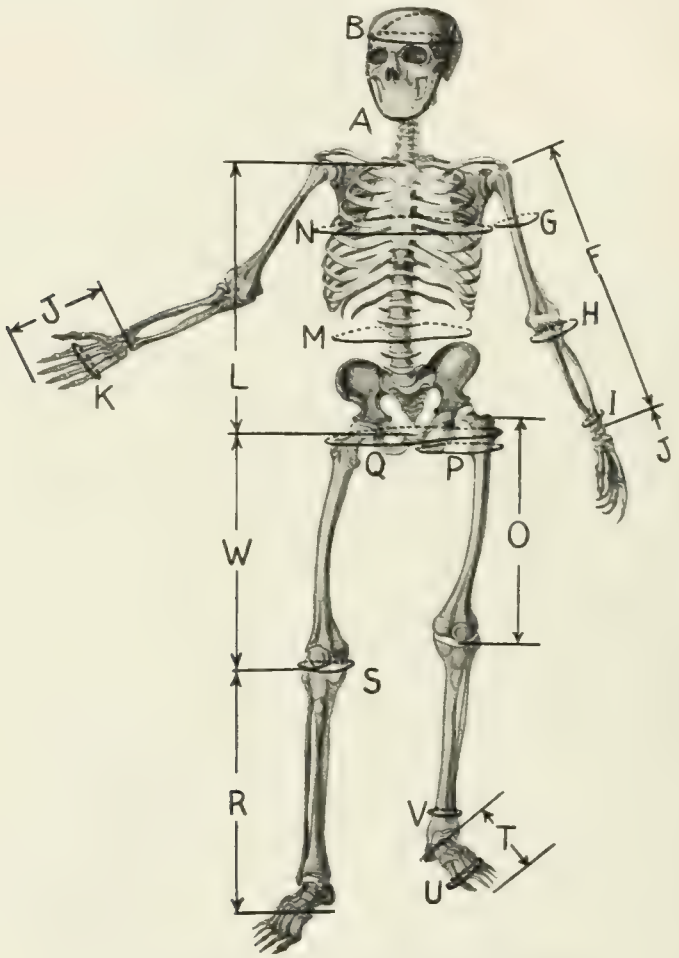


Fig. 1.—Measurements used in "Linear Formula."

are to recalculate previous work in an effort to get more accurate results than are furnished by Meeh's formula we must content ourselves with calculations based on height and weight. A formula such as Meeh's, based on weight alone, can easily give an error of 15 to 20 per cent.,

3. Dr. F. G. Benedict of Boston has called our attention to the fact that this determines the length rather than the height. We have found that as a rule the length is 1 or 2 centimeters greater than the height, but we must remember that height varies 1 to 3 centimeters during the day.

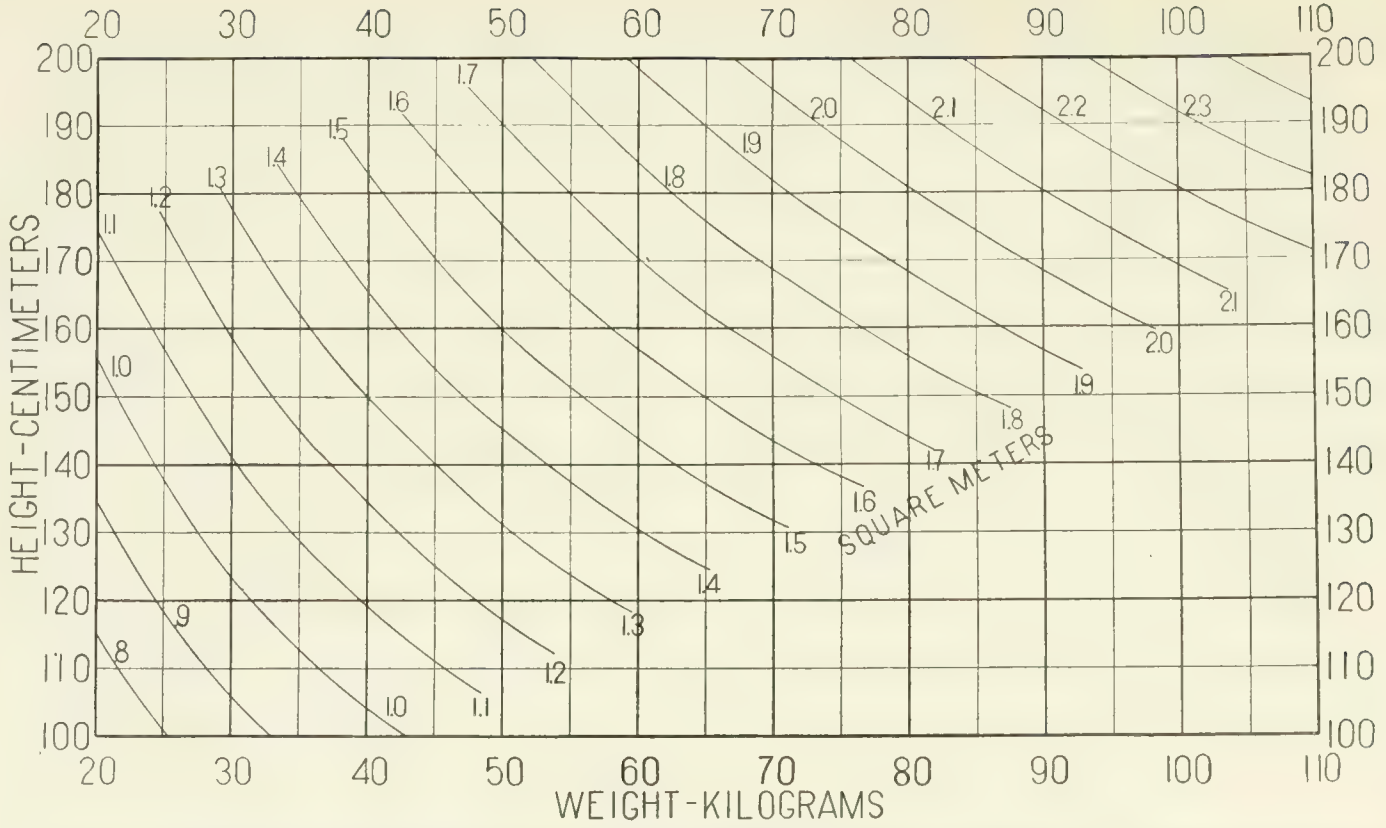


Fig. 2.—Chart for determining surface area of man in square meters from weight in kilograms (Wt.) and height in centimeters (Ht.) according to the formula: Area (Sq. Cm.) $=Wt.^{0.425} \times Ht.^{0.725} \times 71.84$.

but this error is greatly reduced by taking the height into consideration. With people of very unusual body shape there does not seem to be any accurate method simpler than the linear formula with its nineteen measurements. The reason why a consideration of the height does not entirely correct the calculations based on weight becomes apparent when we consider the circumference of the body at various levels. For instance, in the case of R. H. H. the average circumference of the legs was 30.0 cm. and of the thighs 43.9 cm. An increase of 10 cm. in the length below the knees would mean an increase of 600 sq. cm. in surface area, but if the length of the thighs were increased 10 cm. it would mean a gain of 878 sq. cm. Variations in the arms would not affect the height at all.

TABLE 1.—Comparison of Old and New Formulas for Determining Surface Areas of Thighs

Name	Thigh Measurement*		Surface Thighs as Meas., Sq. Cm.	Surface Calc. O(P+Q) 0.508	Error, %	Surface Calc. W(P+Q) 0.552	Error, %
	"O" Cm.	"W" Cm.					
Benny L.	26.4	22.4	1284	1294	+1	1195	− 7
Morris S.	41.7	38.8	3022	3207	+6	3251	+ 7
R. H. H.	47.0	46.0	3712	3512	−5	3745	+ 1
E. F. D. B.	46.3	46.3	3820	3655	−4	3981	+ 4
Mrs. McK.	40.0	32.2	3500	3594	+3	3152	−11
Anna M.	16.0	14.4	478	488	+2	479	+ 0
Gerald S.	44.7	44.9	3002	2677	−11	2927	− 3
Emma W.	45.7	41.7	3324	3448	+4	3425	+ 3
R. H. S.	50.3	46.3	3175	3457	+9	3464	+ 9
Average	....	....	....	....	±5	....	± 5

* Old measurement "O," superior border of great trochanter to lower border of patella. New measurement "W," superior border of pubes to lower border of patella.

A formula to express surface area must naturally be a bi-dimensional formula, as surface involves two dimensions. If we assume that weight is proportional to volume, it is obvious that three dimensions are involved in any expression for weight. Height is, of course, a single dimension. If we attempt to construct a formula for surface area (A) based on weight (W) and height (H), it is obvious that a simple formula such as $A = W \times H \times C$ (C being a constant depending on the units used and the subject to which the formula is to apply) is not logical. In this formula one side, A, is bidimensional and the other side, $W \times H \times C$, involves four dimensions, three from W and one from H. If W is tridimensional, it is obvious that the cube

root of W ($=\sqrt[3]{W}$ or $W^{1/3}$) is undimensional and a formula $A = W^{1/3} \times H \times C$ is logical in that it is bidimensional on both sides. Another bidimensional expression involving W and H would be the square root of $W \times H$ ($\sqrt{W \times H}$ or $W^{1/2} \times H^{1/2}$) because $W \times H$, being four-dimensional, is reduced to a bidimensional expression on taking the square root. A formula based on this method of reduction would be $A = W^{1/2} \times H^{1/2} \times C$.

TABLE 2.—Measurements and Constants for Linear Formula (Measurements Taken with Subject Lying on a Flat Surface)

Head: AB 0.308.
A—Around vertex and point of chin.
B—Coronal circumference around occiput and forehead, just above eyebrows.

Arms: F(G + H + 1) 0.611.*
F—Tip of acromial process to lower border of radius, measured with forearm extended.
G—Circumference at level of upper border of axilla.
H—Largest circumference of forearm (just below elbow).
I—Smallest circumference of forearm (just above head of ulna).

Hands: JK 2.22.
J—Lower posterior border of radius to tip of second finger.
K—Circumference of open hand at the meta-carpo-phalangeal joints.

Trunk (Including neck and external genitals in the male, breasts in female): L(M + N) 0.703.
L—Suprasternal notch to upper border of pubes.
M—Circumference of abdomen at level of umbilicus.
N—Circumference of thorax at level of nipples in the male and just above breasts in the female.

Thighs: O(P + Q) 0.508.
O—Superior border of great trochanter to the lower border of the patella.
P—Circumference of thigh just below the level of perineum.
Q—Circumference of hips and buttocks at the level of the great trochanters.

Or:—Thighs: W(P + Q) 0.552.
W—Upper border of pubes to lower border patella (measured with legs straight and feet pointed anteroposteriorly).
P—As above.
Q—As above.

Legs: RS 1.40.
R—From sole of foot to lower border of patella.
S—Circumference at level of lower border of patella.

Feet: T(U + V) 1.04.
T—Length of foot including great toe.
U—Circumference of foot at base of little toe.
V—Smallest circumference of ankle (just above malleoli).

* Factor 0.558 if F is measured over olecranon with forearm flexed.

Note.—The constants for arms, thighs, etc., when multiplied by the measurements of one side give the surface area for both sides. To find total surface area add the seven parts.

TABLE 3.—Comparison of Various Formulas

Name	Weight, Kg.	Height or Length, Cm.	Measured or Determined by Linear Formula, Area, Sq. Cm.	Area / (Ht.$^{0.5}$ × Wt.$^{0.5}$) = C		Area / (√Ht. × Wt.) = C		Area / (Wt.$^{\frac{1}{2.45}}$ · Ht.$^{\frac{1}{1.48}}$) = C	
				Factor C	Variation from 25.6, %	Factor C	Variation from 167.2, %	Factor C	Variation from 71.84, %
Measured by Molds:									
Benny L.	24.2	110.3	8473	26.7	+4.3	164.0	−2.0	72.30	+0.7
Morris S.	64.0	164.3	16720	25.5	−0.5	163.0	−2.5	70.65	−1.6
R. H. H.	64.1	178.0	18375	25.8	+0.8	171.5	+2.6	73.22	+1.9
E. F. D. B.	74.1	179.2	19000	25.3	−1.2	164.7	−1.5	70.85	−1.3
Mrs. McK.	93.0	149.7	18592	27.2	+6.2	157.5	−5.8	71.70	−0.2
Gerald S.	45.2	171.8	14901	24.4	−4.7	169.2	+1.2	70.36	−2.0
Fab. S.	32.7	141.5	(11869)*	25.5	(−0.5)*	174.2	(+4.0)*	74.37	(+3.5)*
Anna M.	6.27	73.2	3699	27.4	+7.1	172.0	+3.0	75.54	+5.1
Emma W.	57.6	164.8	16451	25.8	+0.8	169.0	+1.1	72.56	+1.0
R. H. S.	63.0	184.2	17981	24.5	−4.3	167.0	0.0	70.58	−1.7
Average	....	.....	.....	....	+3.3	.....	+2.2	.....	+1.7
Measured by Linear Formula									
Edw. B.	62.3	174.0	17270	25.0	−2.3	165.2	−1.2	70.75	−1.5
John K.	65.4	176.0	17610	24.9	−2.7	164.2	−1.7	70.83	−1.4
Alb. S.	66.4	162.2	16720	25.5	−0.5	161.0	−3.7	70.20	−2.3
Wm. S.	44.6	179.0	15450	23.7	−7.4	172.8	+3.3	71.53	−0.4
A. F. C.	69.6	179.4	17960	24.4	−4.7	160.5	−4.0	68.71	−4.4
Wm. A.	63.4	180.0	17940	24.9	−2.7	168.2	+0.6	71.22	−0.8
Mart. C.	44.0	166.8	14370	24.5	−4.3	167.5	+ .1	70.44	−1.9
Jos. U.	40.1	179.0	14520	23.7	−7.4	171.2	+2.3	70.36	−2.1
Wm. Shee.	63.8	171.0	16070	23.5	−8.2	154.8	−7.5	66.06	−8.0
Arthur V.	58.3	155.0	15560	25.8	+0.8	163.3	−2.4	73.02	+1.6
Armon W.	60.8	161.0	15590	23.6	−7.8	156.6	−6.4	67.96	−5.4
Annie T.	26.3	137.0	10460	25.6	0.0	174.0	+4.1	73.60	+2.4
Fred D.	49.3	157.0	13870	24.1	−5.8	157.2	−6.0	67.69	−5.7
Fred D.	40.0	157.0	12960	24.2	−5.5	163.5	−2.3	69.12	−3.8
Edw. T.	50.4	168.0	14830	23.4	−8.6	161.0	−3.7	68.27	−5.0
J. McE.	41.8	166.0	13260	23.1	−9.7	159.0	−4.8	66.67	−7.2
Bart D.	43.5	156.0	13850	25.3	−1.2	168.1	+0.5	71.62	−0.3
Burr Ph.	70.7	169.0	17390	24.9	−2.7	159.0	−4.8	69.01	−3.9
J. D. D. B.	34.5	152.8	12240	24.7	−3.5	168.6	+0.7	70.90	−1.3

TABLE 3.—(*Continued*)

Name	Weight, Kg.	Height or Length, Cm.	Measured or Determined by Linear Formula, Area, Sq. Cm.	Area / (Ht.$^{0.5}$ × Wt.) = C		Area / (Ht. × Wt.) = C		Area / (Wt$^{\frac{1}{2.35}}$ · Ht$^{\frac{1}{1.35}}$) = C	
				Factor C	Variation from 25.6, %	Factor C	Variation from 167.2, %	Factor C	Variation from 71.84, %
Ray M.	30.4	140.5	10840	24.8	−3.1	165.8	−0.8	70.42	−1.9
Harry B.	36.5	146.0	12320	25.4	−0.8	168.6	+0.8	72.01	+0.3
Harry K.	35.9	148.2	12240	25.0	−2.3	167.8	+0.2	71.30	−0.8
Arthur A.	30.6	146.6	11260	24.6	−3.9	167.0	−0.1	70.71	−1.6
Leslie B.	28.5	140.8	10500	24.5	−4.3	166.5	−0.5	70.00	−2.6
Peter N.	63.4	187.7	17950	24.0	−6.2	164.2	−1.8	69.09	−3.8
Max W.	73.2	173.7	18540	25.5	−0.5	164.5	−1.7	71.07	−1.1
Dan O'C.	60.0	167.0	16570	25.4	−0.8	165.7	−1.0	71.12	−1.0
Jack O'C.	31.4	162.8	12040	23.5	−8.2	168.2	+0.6	69.35	−3.5
A. F.	52.6	159.0	14870	25.0	−2.3	162.5	−2.9	69.95	−2.6
G. L.	79.2	175.5	20300	26.9	−5.1	172.2	+3.0	74.70	+4.0
F. C. G.	56.5	173.9	16440	24.7	−3.5	167.4	0.0	70.29	−2.1
L. M.	59.5	170.6	16340	24.6	−3.9	162.1	−3.0	69.30	−3.5
F. G. B.	87.1	182.8	20760	25.8	−0.8	164.5	−1.1	71.22	−0.9

* Measured by adhesive plaster method which gives results about 3.3 per cent. too high. The plus variations would be reduced by this amount.

Comparing the two formulas $A = W^{1/3} \times H \times C$ and $A = W^{1/2} H^{1/2} \times C$, it will be seen that they differ in the relative importance given to W and H. In the former W has less importance and H more importance than in the latter. Meeh's formula $A = W^{2/3} \times C$, failed because H was neglected entirely. Adding H to the formula makes it more nearly applicable to subjects of the same general shape but differing somewhat in relative dimensions, and the best formula involving only W and H will be the one which gives a certain best relative importance to W and H.

Both of the above formulas were carefully investigated by applying them to the nine subjects that had been measured in the laboratory. For these subjects W, H[4] and A are known. In testing a formula the procedure was to solve for C (the only unknown) for each of the ten cases and then to assume the correct constant for the formula to be the average value of the C's so found. The merit of the

4. With about half the subjects this was determined standing. No attempt has been made to correct for the difference between height and length. (See Footnote 3, p. 864.) The largest difference we have found would cause a change of about 1.5 per cent. in the surface area and reading. This is within the limit of accuracy claimed for the Height-Weight Chart.

formula was then judged by the percentage variation of the factors C, as found for the individual cases, from the constant chosen. This percentage variation would also be the percentage error in area in the individual cases if the formula were applied using the chosen constant.

The formulas with H^1 and $H^{1/2}$ both gave rather good results, but it was noticed in a number of cases that the percentage error for the same subject differed in sign for the two formulas. This would indicate that some formula would be better than either of these two if H were raised to some power between ½ and 1.

The formula $A = W^{1/3} \times H \times C$ can also be written $A = W^{1/3} \times H^{1/1} \times C$, bringing it into the same form as $A = W^{1/2} \times H^{1/2} \times C$ and the general form of this formula can be written $A = W^{1/a} \times H^{1/b} \times C$. In order that the expression $W^{1/a} \times H^{1/b} \times C$ may remain bidimensional it is only necessary that $3/a \times 1/b = 2$, as it does in the two cases considered. For an intermediate equation it is obvious that (b) must be greater than 1 but less than 2. A value of $b = 1.25$ would give $a = 2.5$ and the formula would be $A = W^{1/2.5} \times H^{1/1.25} \times C$. This formula when tested gave very much better results than either of the others, but to find the best values of "a" and "b" it was necessary to explore formulas having a number of other combinations of "a" and "b" and then to interpolate graphically.

The best values of "a" and "b" were found to be $a = 2.35$ and $b = 1.38$ giving the formula the final form of $A = {}^{1/2.35} \times H^{1/1.38} \times C$ or $A = W^{0.425} \times H^{0.725} \times 71.84$. This formula can be solved by logarithms as follows:

$$\text{Log. } A = \text{Log. } W \times 0.425 + \text{Log. } H \times 0.725 + 1.8564.$$

1.8564 is a constant equal to Log. C.

In order to make this somewhat complicated formula easy of application a chart has been constructed (Fig. 2). By means of this it is possible to find the approximate surface area at a glance. The ordinates represent the height in centimeters, the abscissae the weight in kilograms. The point of intersection of these lines is found for any given subject and the surface area in square meters read off on the curved lines by interpolation. The second decimal place, which is never accurate, is estimated by the distance of the point from the nearest curved line. For instance, if the man were 150 centimeters tall and weighed 60 kilograms, the approximate surface area would be 1.55 square meters.

The large plus error in the constant employed by Meeh[5] has been established by the previously quoted works of Bouchard, Lissauer, Sicheff, Lassabliere and ourselves. According to our calculations the

5. Meeh: Ztschr. f. Biol., 1879, xv, 425.

average error in Meeh's constant is about 15 per cent. Instead of a uniform figure of 12.312, the "constant" should average about 10.5, varying between 12.3 for the greatly emaciated and 9.0 for the very stout. We must remember that figures for the calories per square meters of body surface will average 15 per cent. smaller when Meeh's formula is used then when the linear formula or the new Height Weight Formula" is employed.

SUMMARY AND CONCLUSIONS

The method of calculating the surface area from the so-called "Linear Formula" is given with a slight correction in the factor for the arms and an alternative measurement for the thighs. A simpler "Height-Weight Formula" has been devised to estimate the surface of subjects if only their height and weight be known. This is expressed in the terms $A = W^{0.425} \times H^{0.725} \times C$. A being the surface area in square centimeters, H the height in centimeters, W the weight in kilograms and C the constant, 71.84. A chart has been plotted from this formula so that the approximate surface area may be determined at a glance.

We may estimate the errors in the various formulas as follows: "Linear Formula" and "Height-Weight Formula," maximum $\pm$ 5 per cent., average $\pm$ 1.5 per cent., Meeh's Formula, maximum + 30 per cent., average + 15 per cent. In general the maximum figures apply only to those of unusual shape, while with those of average body form the average error will seldom be exceeded.

Converse Hall—477 First Avenue.

CLINICAL CALORIMETRY

ELEVENTH PAPER

A COMPARISON OF THE METABOLISM OF MEN FLAT IN BED AND SITTING IN A STEAMER CHAIR*

G. F. SODERSTROM, A. L. MEYER, M.D.
AND
E. F. DU BOIS, M.D.
NEW YORK

This paper and those which follow it are based on results obtained with the Sage calorimeter, which was described a year ago in the first two papers of the series. At that time the policy was adopted of publishing all the alcohol checks to show the accuracy of the apparatus throughout the year. It gives considerable satisfaction to report that the uniformly good results previously obtained have been repeated in this, the third season in which the calorimeter has been used. After a period of several weeks needed to put the apparatus in order, a good check was made Oct. 22, 1914, and not till then were the experiments begun. Although there was no reason to suspect trouble with the apparatus, tests were made Nov. 28, 1914, Jan. 1, 1915 and also on May 19, 1915, after the last experiment for the season was completed. The results are recorded in Table 1 in which it will be seen that the total errors were as follows: heat, + 0.51 per cent., oxygen —0.51 per cent., carbon dioxid —0.36 per cent., water + 3.13 per cent. The respiratory quotient averaged 0.666, while the theoretical quotient is 0.6667.

Since the publication of Paper 2[1] a new valve has been designed by one of the authors (G. F. S.) and has been attached to the absorber table, with most satisfactory results. The three-way valves by means of which the air current was switched from one set of absorbing bottles to the other required constant attention to prevent leaks. The new valves have been used in about ninety experiments and have required repairs but once. The details are shown in Figure 1.

The calorimeter bed has been the subject of much experimentation. The oak frame on skids has proved satisfactory from the start, but the springs under the subjects sagged too much and the blanket covering

* Submitted for publication Feb. 4, 1916.

* From the Russell Sage Institute of Pathology, in Affiliation with the Second Medical Division of Bellevue Hospital.

1. Riche and Soderstrom: Chemical Calorimetry, Paper 2, THE ARCHIVES INT. MED., 1915, xv, 805.

the springs stored too much heat. A waterproof canvas, substituted for the springs, was more comfortable, but heat was accumulated underneath the subject and was suddenly liberated whenever he moved. This made the heat control difficult. During the last year a comfortable hammock made of fish net has given excellent results. Comparatively little heat is banked up underneath the man and when he turns over the liberation of heat is only one half or three quarters as great as in previous years to judge from the expansion of air in the box. This means that a given reading on the work-adder in the season of 1914-1915 indicates a little more activity on the part of the subject than the same reading in previous years.

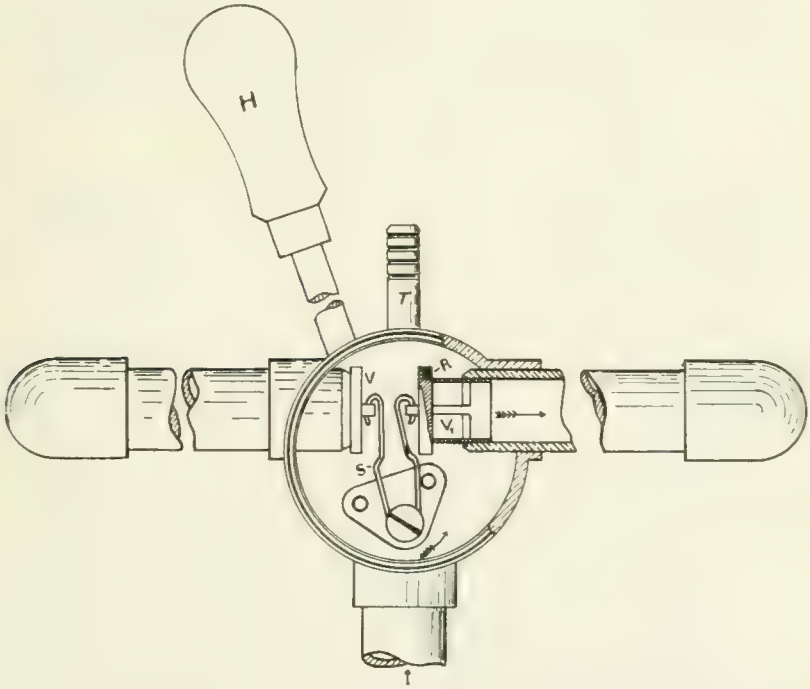


Fig. 1.—Double throw valve for absorber table: H, handle; T, tube through which sample of air can be removed; S, piano wire spring to open and close valves V and V_1; R, rubber washer acting as seat for valve.

Figure 2 shows the bed with the oak frame and hammock. Figure 3 shows the steamer chair used after Jan. 8, 1915. It is very comfortable for the average subject, and even some of those who were not orthopneic preferred it to the bed.

In recording the movements of the spirometer at the close of each hour we have used a pen (Fig. 4) which enables us to dispense with smoked paper. A glass tube a little more than 2.5 cm. long and 9 mm. in diameter is sealed at one end. The other end is closed by means of

cork and sealing wax, through which passes a fine capillary tube bent at a right angle. The capillary passes nearly to the bottom of the tube. The tube is filled with ink, containing a little glycerin. This simple apparatus seems to work even better than the expensive article of commerce which has a platinum tube.

When the calorimeter was planned it was built high enough at one end to allow a man to sit upright. This was essential if orthopneic, cardiac or nephritic patients were to be studied. It soon became evident

Fig. 2.—New calorimeter bed.

that normal subjects should be studied while lying flat and also while sitting with a back rest to serve as controls. The form and accuracy of the Sage calorimeter seemed to lend itself particularly well to this investigation, which requires a greater delicacy of technic than has previously been available.

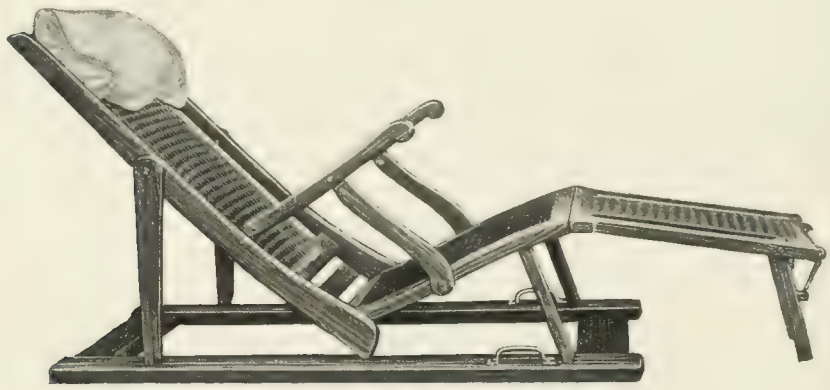


Fig. 3.—Steamer chair for calorimeter.

Katzenstein[2] in 1891 found that the metabolism of his subjects was higher when standing than when lying and that the increase was comparatively slight if the man were standing in a comfortable relaxed position. Winternitz and Pospischil[3] found the carbon dioxid output

2. Katzenstein, G.: Ueber die Einwirkung der Muskeltätigkeit auf den Stoffwechsel der Menschen, Arch. f. d. ges. Physiol., 1891, xlix, 330.

3. Winternitz and Pospischil: Ueber den respiratorischen Stoffwechsel unter thermischen und Mechanischen Einflussen, Bl. f. klin. Hydrotherapie, 1893, 3, 7, 30, 49, 62.

lowest while lying, higher while sitting and still higher while standing. Some of their quotients are so low as to suggest doubts as to the technic. Johansson[4] determined the carbon dioxid production with scrupulous care to avoid the disturbing influences of muscular movement. He found that the output was about 6 per cent. higher while sitting than while lying, but he gives no details as to the exact postures used. Widlund[5] found no apparent rise in metabolism when the man stood if the muscular relaxation were complete. Benedict and Carpenter[6] have compared the metabolism of their subjects in two different calorimeters. Their bed calorimeter is smaller than the Sage instrument and the subjects lie flat during the experiments, are very quiet and often go to sleep. Their chair calorimeter contains a comfortable armchair, tilted slightly backwards but without a head rest. In this chamber the subjects are not absolutely quiet, but are allowed to read. The

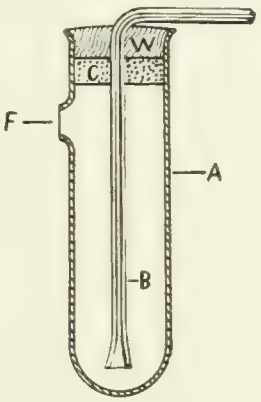


Fig. 4.—Capillary writing pen: A, glass reservoir for ink; F, opening for filling; C, cork; W, sealing-wax; B, capillary glass tube.

matter is critically treated by Benedict and Joslin,[7] who conclude that the increase in metabolism of a subject while sitting in a chair and awake over that when lying asleep varies from 20 to 30 per cent. The question was further studied by Emmes and Riche[8] in the same labora-

4. Johansson, J. E.: Ueber den Tageschwankungen des Stoffwechsels und der Körpertemperatur im nüchternen Zustand und vollstandlichen Muskelruhe, Skand. Arch. f. Physiol., 1898, viii, 85.

5. Widlund, K. E.: Untersuchung des Verhaltnisses zwischen CO_2 Produktion in Rühelage und im stehenden Stellung, Skand. Arch f. Physiol, 1905, xvii, 290.

6. Benedict and Carpenter: Metabolism and Energy Transformation of Healthy Man During Rest, Carnegie Institution of Washington, Pub. 126, 1911, p. 242.

7. Benedict and Joslin: Metabolism in Diabetes Mellitus, Carnegie Institution of Washington, Pub. 136, 1910, p. 175.

8. Emmes, L. E., and Riche, J. A.: The Respiratory Exchange as Affected by Body Position, Am. Jour. Physiol., 1911, xxvii, 406.

tory, using the Benedict Universal Respiration Apparatus to which the subjects were attached by means of nose pieces. They found the oxygen consumption averaged 7.6 per cent. higher when they were sitting upright in a chair with the head supported than when lying flat. This they considered due primarily to the difference in the internal muscular activity necessitated by the sustaining of body parts. They call attention to the fact that the pulse rate is 5 to 10 per cent. higher when sitting. Higgins,[9] also of the Nutrition Laboratory, studied the effect of posture on the tension of carbon dioxid in the alveoli, and found it highest with the subject lying on his back or side, lower in the Trendelenburg and semireclining position, still lower while sitting erect and lowest while standing.

DESCRIPTION OF SUBJECTS OF EXPERIMENTS

John L., 44 years old, 174.7 cm. tall, normal control, history given in Paper 4.[10] March 26, 1914, he lay flat on the canvas bed. April 3 he sat propped up in bed at an angle of about 50 degrees, leaning against a firm back rest, padded with pillows, which supported his head.

Albert G., 24 years old, 162.2 cm. tall, normal control. He is a laborer, born in Italy. He remembers no illnesses except a slight skin eruption fourteen years ago. His health is good but he has been out of work for some time. He is short, stocky, fairly muscular, with little fat. Heart and lungs normal. Admitted to the metabolism ward Dec. 14, 1914, discharged Jan. 14, 1915. From January 4 to 14 he had a very mild sore throat, with slight afternoon fever. January 13 at 10 a. m., he was given subcutaneously a dose of New York City Board of Health typhoid vaccine consisting of one-half billion dead bacilli. There was a slight normal reaction with moderate swelling at the site of injection.

The young Italian was rather neurotic, and after a couple of weeks of enforced idleness in the ward began to develop imaginary pains. He left the hospital in high dudgeon, but when his wages were spent in the course of the next two weeks he returned asking for his job as normal control.

December 21, lying flat in bed, he was unusually quiet, sleeping twenty-four minutes in the first hour and about six minutes in the second. Two days later, propped up at an angle of about 45 degrees with the back rest, he was not so quiet. The third period had to be discarded from the calculations because he slid down in the bed until the body was at about half its original angle. December 28 he was in the calorimeter for two periods, each one and one-half hours long. He was lying flat and very quiet, dozing most of the time. December 30 an experiment was made after the ingestion of 79 gm. of olive oil. January 4 and 6 tests were made after 115 gm. commercial glucose. On the eighth a three hour basal determination was made. He slept fifty-five minutes in the first hour and was somewhat restless in the other hours. The next day he was in the calorimeter, sitting in the steamer chair which had just been finished. In the first hour he was somewhat restless, in the second hour quiet. Unfortunately the urine specimen was lost on this day.

R. H. S., man, 21½ years old, chemist, normal control. Except for measles, scarlet fever and a broken arm in childhood he has never been sick in bed. He

9. Higgins, H. L.: The Influence of Food, Posture and Other Factors on the Alveolar Carbon Dioxid Tension in Man, Am. Jour. Physiol., 1914, xxxiv, 114.

10. Gephart and DuBois: Clinical Calorimetry, Paper 4, THE ARCHIVES INT. MED., 1915, xv, 835.

TABLE 1.—Alcohol Checks

Date	Hour	Heat				Oxygen			Carbon Dioxid			Water			R. Q. Theory, (0.667)
		Alcohol Burned, Gm.*	Theory, Cal.	Found, Cal.	Error, %	Theory, Gm.	Found, Gm.	Error, %	Theory, Gm.	Found, Gm.	Error, %	Theory, Gm.	Found, Gm.	Error, %	
10/22/14	1	12.22	78.14	77.14	−1.2	23.02	22.56	−1.9	29.01	20.92	−0.8	13.82	15.32	+10.8	0.673
	2	11.96	76.48	75.19	−1.6	22.52	22.77	+1.1	20.64	20.41	−1.1	13.84	14.64	+5.7	0.652
	3	11.93	76.29	75.47	−1.0	22.47	21.85	− 2.7	20.59	20.25	− 1.6	13.81	14.33	+3.7	0.674
Average.....	...	.....	76.97	75.93	−1.3	22.69	22.39	−1.3	20.77	20.53	1.1	13.82	14.76	+6.8	0.666
11/27/14	1	11.96	76.49	77.74	+1.6	22.52	22.17	−1.5	20.64	20.55	−0.4	13.84	14.14	+2.1	0.674
	2	12 23	78.21	78.36	+0.2	23.03	23.04	±0.0	21.11	21.06	- 0.2	14.15	14.19	+0.2	0.664
	3	12.56	80.32	80.84	+0.6	23.65	23.40	- 1.0	21.68	21.47	- 0.9	14.53	14.60	+0.4	0.667
Average.....	. .	.....	78.34	78.98	+0.8	23.07	22.87	−0.8	21.14	21.03	- 0.5	14.17	14.31	+1.0	0.668
1/18/15	1	13.67	87.41	89.35	+2.2	25.74	25.89	+0.9	23.60	23.19	- 1.7	15.82	16.34	+3.2	0.652
	2	13.54	86.58	88.99	+2.7	25.50	25.81	+1.2	23.37	23.54	+0.7	15.67	16.27	+3.8	0.663
	3	13 62	87.09	87.17	+0.06	25.65	24.99	−2.5	23.51	23.13	−1.6	15.76	15.82	+0.3	0.673
Average.....	...	.....	87.03	88.50	+0.5	25.63	25.56	- 0.2	23.49	23.29	- 0.8	15.75	16.14	+2.4	0.663
5/19/15	1	10.46	66.89	67.23	+0.5	19.70	19.85	+ 0.7	18.05	18.19	+0.7	12.10	12.52	+3.4	0.666
	2	10.41	66.57	66.21	−0.5	19.60	19.35	- 1.27	17.97	17.75	−1.2	12.04	12.29	+2.0	0.667
	3	10.20	65.23	66.72	+2.2	19.21	19.54	+1.72	17.21	18.08	+ 5.0	11.80	12.12	+2.7	0.672
Average.....	...	.....	66.23	66.72	+0.7	19.50	19.58	+0.4	17.74	18.01	+ 1.5	11.98	12.31	+2.7	0.669
Total.....	...	.....	925.69	930.41	+0.51	272.61	271.22	- 0.51	249.46	248.54	−0.36	167.18	172.58	+3.13	Av. 0.666+

* In most of the tests the solution contained 90.32% by weight of ethyl alcohol.

TABLE 2.—DATA OF—

Subject, Date, Weight, Surface Area Linear Formula	Period	End of Period Time	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N. per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
John L.	Prelim.	11:20	.....	.....	....	.....	.....	.....	.....
3/26/14									
70.94 Kg.	1	12:20	21.12	19.51	0.79	25.77	0.363	64.65	66.00
	2	1:20	21.37	19.62	0.79	24.56	0.363	65.10	68.26
	3	2:20	21.07	19.97	0.78	24.01	0.363	65.85	66.72
								195.20	
John L.	Prelim.	12:05	.....	.....	....	.....	.....	.....	.....
4/3 14									
70.90 Kg.	1	1.05	20.36	18.33	0.81	22.90	0.347	61.08	61.79
	2	2:05	19.94	18.47	0.79	23.66	0.347	61.19	63.45
								122.27	
Albert G.	Prelim.	11:13	.....	.....	....	.....	.....	.....	.....
12 21/14									
66.03 Kg.	1	12:13	24.32	20.68	0.86	31.28	0.60	69.31	75.78
1.67 Sq. M.	2	1:13	25.97	20.96	0.90	31.59	0.60	71.08	78.38
	3	2:13	24.31	21.22	0.83	31.86	0.60	70.73	78.17
								211.12	
Albert G.	Prelim.	11:09	.....	.....	....	.....	.....	.....	.....
12 23/14									
63.03 Kg.	1	12:09	24.73	20.43	0.88	23.81	0.636	68.89	62.75
1.63 Sq. M.	2	1:09	23.44	20.22	0.84	26.68	0.636	67.53	68.59
	3	2:09	26.11	23.15	0.82	28.22	0.636	77.07	69.69
								213.49	
Albert G.	Prelim.	11:05	.....	.....	....	.....	.....	.....	.....
12/28/14									
65.35 Kg.	1	12:35	34.28	28.96	0.86	39.12	0.731	97.54	112.03
1.66 Sq. M.	2	1:05	35.80	29.23	0.89	39.24	0.731	99.06	107.08
								196.60	
Albert G.	Prelim.	11:21	.....	.....	....	.....	.....	.....	.....
1/8/15									
66.33 Kg.	1	12:21	22.43	19.88	0.82	27.86	0.661*	66.09	68.19
1.67 Sq. M.	2	1:21	25.06	20.38	0.89	29.56	0.518*	69.16	72.48
	3	2:21	24.92	22.81	0.79	30.70	0.518	75.51	71.82
								210.76	
Albert G.	Prelim.	11:13	.....	.....	....	.....	.....	.....	.....
1/9/15									
65.85 Kg.	1	12:13	25.35	21.50	0.86	33.84	.....	72.89	75.78
1.67 Sq. M.				19.07	0.90	32.76	.....	65.32	76.38
	2	1:13	23.62					138.21	
				.....	....	.....	.....	.....	.....
R. H. S.	Prelim.	11:40	.....	19.95	0.85	26.28	0.478	66.98	79.97
4/19/15									
64.36 Kg.	1	12:40	23.21	20.87	0.83	26.25	0.478	69.82	77.61
1.83 Sq. M.	2	1:40	23.79					136.80	

* Calculations for first period were based on a mean of these two figures.

—Calorimeter Experiments

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
.....	37.11	..	....	....	..	..	..	....	.....	Basal
52.79	36.89	61	13.0	0.78	15	62	23	0.90	30.64	Flat in bed
68.56	36.94	55	13.0	0.79	15	61	24	0.90	30.85	
62.04	36.88	57	38.7	0.76	15	69	16	0.90	31.21	
183.30										
.....	36.89	..	....	....	..	..	..	....	.....	Propped up with back rest
57.31	36.82	59	23.0	0.81	15	55	30	0.86	28.96	
60.47	36.80	62	27.0	0.78	15	63	22	0.86	29.01	
117.78										
.....	37.11	..	....	....	..	..	..	....	.....	Basal, flat in bed
69.44	37.00	58	12.5	0.87	23	34	43	1.05	34.45	Asleep 24 min.
72.03	36.89	54	14.6	0.93	22	19	59	1.08	35.33	Asleep 6 min.
73.58	36.85	52	14.7	0.84	22	42	35	1.07	35.15	
215.05										
.....	37.13	..	....	....	..	..	..	....	.....	Propped up at angle of 45 deg.
53.62	36.96	54	17.1	0.91	25	23	52	1.10	35.33	Quiet
68.25	36.96	54	14.6	0.86	25	36	39	1.07	34.63	Quiet
71.24	37.01	56	19.0	0.83	22	45	33	1.22	39.52	Slid down in bed
193.11										
.....	36.79	..	....	....		..	..	....	.....	Basal. Flat
116.76	36.85	52	12.2	0.88	20	33	48	1.00	32.55	Dozed
96.84	36.69	53	19.0	0.91	20	25	56	1.01	33.05	Dozed. Periods 1½ Hrs. long
213.60										
.....	36.74	..	....	....	..	..	..	....	.....	Basal, flat in bed
65.19	36.63	58	3.5	0.83	24	44	32	1.00	32.77	Asleep 55 min.
70.68	36.62	56	29.0	0.92	20	22	58	1.07	35.09	Restless
73.59	36.68	55	27.2	0.79	18	58	23	1.14	37.44	Restless
209.46										
.....	37.06	..	....	....	..	..	..	....	.....	In steamer chair
66.58	36.90	62	18.0	....	..	..	..	1.11	36.30	Restless
73.98	36.84	59	14.0	....	..	..	..	0.99	32.55	Quiet Urine spec. lost
140.56										
.....	37.12	..	....	....	..	..	..	....	.....	Basal, flat in bed
72.65	36.99	60	1.0	0.86	19	39	243	1.04	33.88	Almost motionless
71.40	36.89	60	6.0	0.84	18	45	37	1.09	35.32	Almost motionless
144.05										

TABLE 2.—

Subject, Date, Weight, Surface Area Linear Formula	Period	End of Period Time	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	per Hour, Urine N. Gm.	Calorimetry, Indirect Cal.	Eliminated, Heat Cal.
R. H. S.	Prelim.	11:22	.....	.....	....	.....	.....	.....	.....
4 21/15									
63.35 Kg.	1	12:22	21.55	18.69	0.84	24.82	0.393	65.76	76.49
1.78 Sq. M.	2	1:22	21.94	18.84	0.85	25.37	0.393	58.54	76.96
								124.30	
E. F. D. B.	Prelim.	11:17	.....	.....	....	.....	.....	.....	.....
5 6/15									
74.64 Kg.	1	12:17	23.43	21.39	0.80	31.59	0.528	70.75	70.84
1.91 Sq. M.	2	1:17	23.69	22.04	0.78	32.82	0.528	72.78	73.96
								143.53	
E. F. D. B.	Prelim.	11:18	.....	.....	....	.....	.....	.....	.....
5/7.15									
74.20 Kg.	1	12:18	23.12	20.51	0.82	33.52	0.593	68.22	76.92
1.90 Sq. M.	2	1:18	23.45	20.73	0.82	31.68	0.593	68.96	75.07
								137.18	
William A.	Prelim.	11:13	.....	.....	....	.....	.....	.....	.....
1/25/15									
63.44 Kg	1	12:13	25.32	20.31	0.91	34.45	0.382	69.44	72.58
1.80 Sq. M.	2	1:13	24.08	20.86	0.84	32.15	0.382	70.14	73.06
	3	2:13	24.45	22.02	0.81	31.11	0.382	73.44	73.48
								213.02	
William A.	Prelim.	10:40	.....	.....	....	.....	.....	.....	.....
1/27/15									
63.00 Kg.	1	11:40	24.37	21.08	0.84	32.50	0.390	70.86	73.83
1.74 Sq. M.	2	12:40	25.01	22.17	0.82	32.37	0.390	74.09	75.33
	3	1:40	24.75	23.05	0.78	33.53	0.390	76.38	78.06
								221.33	
Theodore S.	Prelim.	11:10	.....	.....	....	.....	.....	.....	.....
1/28/14									
59.52 Kg.	1	12:10	23.13	20.30	0.83	39 03	0.454	67.86	77.28
	2	1:10	23.98	21.43	0.81	38.26	0.454	71.40	76.66
Theodore S.	Prelim.	11:15	.....	.....	....	.....	.....	.....	.....
1/30/14									
59.44 Kg.	1	12:15	21.66	18.76	0.84	36.00	0.385	62.97	73.11
	2	1:15	22.80	20.18	0.82	37.75	0.385	67.48	73.83
Theodore S.	Prelim.	11:46	.....	.....	....	.....	.....	.....	.....
2 5 14									
60.28 Kg.	1	1:16	34.63	31.59	0.80	50.61	0.538	105.10	118.65
	2	2:16	22.82	20.53	0.81	32.00	0.538	68.47	72.40
Theodore S.	Prelim.	11:50	.....	.....	....	.....	.....	.....	.....
2/9/14									
61.15 Kg.	1	12:50	21.11	18.41	0.83	21.14	0.394	61.66	56.93
	2	1:50	22.34	19.11	0.85	22.55	0.394	64.30	60.88
Theodore S.	Prelim.	11:10	.....	.....	....	.....	.....	.....	.....
2/13 14									
61.99 Kg.	1	12:10	24.54	20.49	0.87	26.73	0.391	69.38	70.40
	2	1:10	24.35	21.15	0.84	33.09	0.391	71.02	75.79

—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
.....	37.00	..	....	....	..	..	..	....	.....	In steamer chair
67.20	36.83	62	1.0	0.83	16	49	36	1.04	33.60	Almost motionless
78.30	36.86	57	6.0	0.86	18	39	43	0.92	29.91	Almost motionless
145.50										
.....	36.99	..	....	....	..	..	..	....	.....	Basal, flat in bed
69.89	36.98	57	10.0	0.79	20	57	23	0.95	32.40	Very quiet
75.52	37.01	57	7.0	0.78	19	63	18	0.98	33.32	Very quiet
145.41										
.....	36.92	..	....	....	..	..	..	....	.....	In steamer chair
67.38	36.76	57	9.0	0.83	23	45	33	0.92	32.12	Quiet
78.32	36.83	55	12.0	0.83	23	45	33	0.93	32.47	Quiet
145.70										
.....	36.96	..	....	....	..	..	..	....	.....	Cardiac patient; flat in bed
62.29	36.77	62	20.0	0.93	15	20	65	1.10	35.47	Restless
69.48	36.71	60	11.0	0.85	14	68	18	1.10	35.82	Fairly quiet
70.55	36.66	62	10.0	0.81	14	62	24	1.16	37.51	Quiet
202.32										
.....	.....	..	....	....	..	..	..	....	.....	In steamer chair
66.72	36.76	66	10.0	0.85	15	44	42	1.13	36.36	Quiet
72.33	36.71	66	11.0	0.82	14	53	33	1.18	38.01	Quiet
73.06	36.62	..	21.0	0.78	14	65	22	1.21	39.19	Fairly quiet
212.11										
.....	37.14	..	....	....	..	..	..	....	.....	Cardiac patient; flat on back
89.92	36.94	49	21.0	0.84	18	46	36	1.14	36.14	Restless
71.30	36.93	50	23.0	0.82	17	52	31	1.20	38.03	Restless
.....	37.10	..	....	....	..	..	..	....	.....	Propped up in bed at angle of about 30 deg.
70.46	37.05	53	1.9	0.85	16	44	40	1.06	33.58	
75.61	37.13	52	0.9	0.83	15	51	34	1.14	35.99	
.....	37.03	..	....	....	..	..	..	....	.....	Flat on back; quiet both periods. Pain in hand at 12:43. Periods 1½ Hrs.
86.70	36.87	50	10.0	0.80	14	60	26	1.16	37.09	
72.40	36.94	47	0.6	0.81	14	56	30	1.14	36.26	
.....	37.06	..	....	....	..	..	..	....	.....	Propped up in bed at angle of 50 deg. Quiet both periods
64.71	36.83	49	6.7	0.84	17	45	38	1.01	32.28	
67.15	36.86	46	3.7	0.86	16	40	44	1.05	33.67	
.....	37.01	..	....	....	..	..	..	....	.....	Flat on back
66.94	36.95	54	3.5	0.88	15	34	51	1.12	35.99	Quiet
75.32	36.95	55	5.5	0.84	15	45	40	1.15	36.84	Quiet

is accustomed to take moderate exercise and his general health is fair. This last year he has been doing much night work, has taken no exercise, and has lost about 5 pounds in weight. He is very tall, 184.2 cm. and very thin, but not emaciated. His measurements and surface area are given in detail in Paper 9 of this series. His heart and lungs, etc., are normal.

April 19, 1915, he was in the calorimeter flat in bed for two hours to determine the basal metabolism, and two days later was in the steamer chair for a similar period. On both days he was awake but almost motionless.

E. F. D. B., man, 33 years old, a normal control, whose history is given in Paper 4[10] of this series. May 6, 1915, he was in the calorimeter flat in bed. Except for a small cup of black coffee without sugar, he had taken no food since 7:30 p. m. The steamer chair experiment, owing to a sudden change in plans, had to be made the next day. Unfortunately the subject had eaten a Welsh rarebit at 11 p. m., so it is possible that there was a slight specific dynamic action increasing the metabolism. He was quiet in both experiments.

CARDIAC PATIENTS

Theodore S., 32 years old, coachman, born in Sweden. Admitted Jan. 17, 1914, discharged February 22. Diagnosis, mitral stenosis, cardiac hypertrophy and dilatation, auricular fibrillation.

History.—Pneumonia when 6 years old, no rheumatism. Four or five years prior to admission the patient began to have shortness of breath on exertion. Three years previous to admission this compelled him to look for an easy job, but he was able to carry trunks upstairs until eight months prior to admission. For the previous two weeks the dyspnea had confined him to bed.

Physical Examination.—Of medium build, 169 cm. tall, well nourished and fairly muscular. He is slightly dyspneic, the lips are a deep red color, with a slight purplish tint. He has an occasional cough. The apex is in the fifth costal interspace 12 cm. from the midline, the left limit of dulness 14.5 cm. from midline, the right limit in the fourth space 4 cm. from midsternum. The action is slow and very irregular in force and frequency. Phlebograms show auricular fibrillation. At the apex is heard the presystolic murmur to which Mackenzie and Lewis have recently called attention. The first sound is sharp and short, the second sound faint, followed immediately by a loud, rough, rumbling murmur which diminishes during diastole, lasting through the short diastoles but followed by a period of silence in the long pauses. The pulse is small, the arteries palpable. There are a few subcrepitant râles at the bases of the lungs. The Wassermann reaction is negative. By January 26 all dyspnea had disappeared and there was not the slightest trace of orthopnea. He was able to sit in a chair without fatigue. There was no edema.

Experiments.—January 28, basal experiment flat in bed. The patient was anxious to cooperate but he was of timid nature and during this first observation was a little anxious. His skin was cold and clammy at the start and he sweated profusely while in the calorimeter. January 30 he was propped up on the calorimeter bed at an angle of about 30 degrees. He was quieter than before. February 5 he was in the calorimeter flat in bed. Just as the first period was being ended he had a slight pain in his hand which caused him to sweat. This suddenly expanded the air in the box and raised the work adder 5 cm. The first period was prolonged one-half hour, by which time things had come into equilibrium. February 9 he was propped up with the back rest at an angle of about 50 degrees and made very comfortable with pillows at his back and under his knees. February 13 a third experiment with the patient flat in bed was made. He was comfortable and quiet but apparently began to sweat a little when signalled to lie quiet at the end of each period.

February 16 the systolic blood pressure was 145 mm. lying down and 142 mm. when sitting up at an angle of about 45 degrees. February 22 he was discharged in good condition and was able to walk up two flights of stairs slowly

without dyspnea. March 4 he was readmitted with a sharp attack of bronchopneumonia from which he recovered, leaving the hospital on the 27th of that month.

William A., 24 years old, laborer. Admitted to the hospital Dec. 28, 1914, discharged Jan. 30, 1915. Diagnosis, aortic insufficiency, cardiac hypertrophy and dilatation. History. Has had measles, pneumonia, rheumatism and urethritis and has had frequent attacks of tonsillitis. December 25 he had a sudden sharp pain in the side. The following night he was very orthopneic and had a great deal of palpitation. He complains also of weakness and cough.

TABLE 3.—Summary of Calorimeter Experiments on Body Posture

Subjects	Age, Years	Weight, Kg.	Average Pulse	R. Q.	Average Calories per Hour		Posture
					Indirect Calorimetry	Direct Calorimetry	
Normals							
John L.	44						
3/26/14	..	70.94	58	0.78	65.20	61.10	Lying*
4/3/14	..	70.90	61	0.80	61.14	58.80	Sitting up
Albert G.	24						
12/21/14	..	66.03	54	0.86	70.37	71.68	Lying
12/23/14	.	63.03	54	0.85	71.16	64.37	Sitting up
12/28/14	..	65.35	73	0.88	98.30	100.80	Lying
1/8/15	..	66.33	56	0.84	70.25	69.82	Lying
1/9/15	..	65.85	61	0.88	69.10	70.28	Sitting up
R. H. S.	21						
4/19/15	..	64.86	60	0.84	68.40	72.03	Lying
4/21/15	..	63.35	59	0.84	62.15	72.75	Sitting up
E. F. D. B. ..	33						
5/6/15	..	74.64	57	0.79	71.77	72.71	Lying
5/7/15	..	74.20	56	0.82	68.59	72.85	Sitting up
Cardiacs							
William A. ..	24						
1/21/15	..	63.44	61	0.85	71.01	67.44	Lying
1/27/15	..	63.00	66	0.81	73.78	70.70	Sitting up
Theodore S.	32						
1/28/14	..	59.52	50	6.82	69.63	80.26	Lying
1/30/14	..	59.44	53	0.83	65.23	73.04	Sitting up
2/5/14	..	60.28	49	0.80	86.79	76.01	Lying
2/9/14	.	61.15	48	0.84	62.98	65.93	Sitting up
2/13/14	..	61.99	55	0.85	76.20	71.13	Lying

* Basal—flat in bed.

Physical Examination.—Tall (180 cm.), well developed and well nourished; dyspneic and orthopneic; color pale.

Tonsils swollen and congested. Apex impulse diffuse, left border 13 cm. right border 4 cm. from midline. There is a waterfall diminuendo diastolic murmur and a presystolic roughness considered to be a Flint murmur. The pulse is Corrigan in type.

The temperature, which has been slightly elevated, dropped to normal and the dyspnea and orthopnea disappeared. A blowing systolic murmur became

audible in the aortic region. By January 26 he was able to sit all day in a chair without fatigue.

January 25 he was in the calorimeter flat on his back for three hours, and two days later was in the steamer chair for a similar period.

METHODS OF EXPERIMENTS

The calorimeter and the experimental procedure have been described in Papers 1 to 4 of this series. All the experiments were made in the morning without food, except in a few instances when a small cup of black coffee without sugar was used. When the subjects were flat in bed they were allowed a pillow under the head, and if they desired it, one under the knees.

DISCUSSION OF RESULTS

Each experiment in the sitting posture is controlled by one or more observations on the same individual lying flat in bed, and we might therefore compare the average calories per hour produced under the

TABLE 4.—SUMMARY OF RESULTS

Name	Average Pulse		Average Metabolism, Cal. per Sq. M. per Hour, Meeh		Per Cent. Difference in Semireclining
	Lying	Semireclining	Lying	Semireclining	
Normal Controls					
John L.	58	61	30.90	28.99	—6.1
Albert G	54	58	*34.29	34.71	+1.2*
R. H. S.	60	59	34.60	31.75	—8.2
E. F. D. B.	57	56	32.86	32.29	—1.7
Cardiac Cases					
Theodore S.	51	51	36.73	33.89	—7.7
William A.	61	66	36.27	37.85	+4.4
Average	..	..	.....	.....	—3.0

* Omitting experiment of December 28, averages are: metabolism, lying equals 35.04; per cent. difference equals —1.0.

two conditions. The standard procedure in this laboratory, however, has been to compare the results in terms of calories per square meter of surface area per hour. This latter method will be adhered to, since these experiments will be discussed from other points of view in the following papers. It makes little difference which method is used, as the surface area scarcely changed at all between experiments.

The results are summarized in Tables 3 and 4. It will be seen that the metabolism averaged 3 per cent. lower in the semireclining than in the lying posture. Of the four normal subjects, three showed this lower metabolism very clearly. In one, Albert G., the average figure for the flat experiments is 1.2 per cent. lower, but if the abnormally low result in the experiment of December 28, when he dozed, be

excluded, the balance will be 1.0 per cent. on the other side of the line. It is unfortunate that it was not possible to have more cardiac patients in the series. The mitral case repeatedly showed a lower metabolism when propped up in bed; the aortic patient showed the opposite. Taken as a whole, the differences are so small that we may use the same figure for the average normal metabolism in both postures, and we need hardly change our normal base line when we discuss the experiments on patients who were so orthopneic that they had to use the steamer chair while in the calorimeter.

These results were somewhat surprising as the general opinion in the laboratory was that the heat production would be 5 to 10 per cent. higher in the steamer chair. It must be remembered that previous investigators have used chairs in which the subjects sat upright or nearly upright, in some cases the head being unsupported. All the experimenters agreed that there was some muscular effort needed to maintain the posture and they ascribed to this the increase in heat production. In the orthopneic posture either with back rest or steamer chair as used in these calorimeter experiments, there was complete support of the body and head. No more muscular tension was needed than when the subjects were lying flat and the pillows were so arranged that the men could fall asleep without change in posture. It is quite possible that the diminished pressure on the diaphragm lessened the work of breathing enough to account for the lower metabolism.

On steamers, in clubs, and in those parts of our country where laziness is a science, men assume a semireclining posture with the head, back and feet supported on any convenient object. Patients who are very dyspneic are obliged to sit up and they can sleep only in the semireclining posture. The slight diminution in energy requirement may be a factor in leading them to assume the orthopneic posture, but with many cardiac and nephritic patients this economy is more than offset by increased muscular activity.

SUMMARY AND CONCLUSIONS

The Sage calorimeter in the season of 1914-1915 was fully as accurate as in the previous years. Alcohol checks gave the following total errors: heat + 0.51 per cent., oxygen — 0.51 per cent., carbon dioxid — 0.36 per cent., water + 3.13 per cent. The respiratory quotient averaged 0.666 while the theoretical quotient was 0.6667.

Four normal men and two cardiac patients were studied in the calorimeter lying flat in bed and in the semireclining position propped up with a back rest, or else in a comfortable steamer chair. A total of twenty-one experiments showed that the metabolism averaged 3 per cent. lower in the semireclining posture. One of the cardiacs, and pos-

sibly one of the normal controls, showed a slightly higher metabolism when propped up in bed.

The difference between the results is so small that in the study of pathologic cases we can use the same figures for the average normal metabolism in both postures. In the majority of cases, however, the energy requirement is lower in the orthopneic position.

477 First Avenue.

CLINICAL CALORIMETRY

TWELFTH PAPER

THE METABOLISM OF BOYS 12 AND 13 YEARS OLD COMPARED WITH THE METABOLISM AT OTHER AGES*

EUGENE F. Du BOIS, M.D.
NEW YORK

In the period of development of boys, the years immediately preceding puberty are of especial interest. By this time the figure has lost most of its childish characteristics and the mind has reached a point of great intelligence. Although the individual has scarcely passed the half-way mark in the years of growth, and has only attained half his future weight, yet he resembles the adult much more than he resembles the infant. At this stage the sex glands have not yet begun the rapid development of puberty with its profound effect on the whole organism. Curiously enough there is a sudden increase in the rate of growth which takes place at this time. In fact, we may consider boys in the period of prepubescence as individuals of adult form but of small size, growing rapidly, and as yet scarcely influenced by the internal secretions of the sex glands. The study of their respiratory exchanges may throw light on many problems.

Recent developments in the science of metabolism have emphasized the necessity of using, for purposes of comparison, only those experiments in which the subjects were absolutely quiet. Since the assimilation of food increases the metabolism during four or five hours following a small meal, and five to ten hours after a large one, it is important to use only experiments in which this specific dynamic action is either slight or absent. The necessity for absolute quiet has long been recognized by Johansson and the Zuntz school, but has only been fully appreciated elsewhere for the last five years or so. The observations of Rubner[1] and Sonden and Tigerstedt[2] were made before this was understood, and the children were studied in large respiration chambers where they sat fairly quiet in chairs, eating from time to time, or else, as in the case of Rubner's boys, moving about the room at will. This

* Submitted for publication Feb. 4, 1916.

* From the Russell Sage Institute of Pathology, in Affiliation with the Second Medical Division of Bellevue Hospital.

1. Rubner: Beitrage zur Ernährung im Knabenalter, Berlin, 1902.

2. Sonden and Tigerstedt: Untersuchungen über die Respiration und den Gesamtstoffwechsel des Menschen, Skand. Arch. f. Physiol., 1895, vi, 1.

amount of activity might increase the metabolism anywhere from 10 to 30 per cent. above the resting value, and it is obvious that the results can be compared only with those obtained on other individuals who have shown exactly the same amount of muscular movement. It is for this reason that, while the careful work of the above mentioned observers is of great value in showing the changes during the different ages for a given amount of activity, it cannot be used in comparison with the experiments in which the subjects are quiet.

The classical study of Magnus-Levy and Falk[3] established the fact that the metabolism is high during childhood and low after the onset of old age. These observers studied twenty-five children, twelve old men and women and twenty-five of intermediate ages. They used the Zuntz-Geppert apparatus, making several short experiments on each subject in the morning before breakfast, the individual lying at complete rest on a couch. It so happened that they included no boys between the ages of 11 and 14 in their list.

The metabolism during infancy has been well studied by Howland,[4] Schlossmann and Murschhauser,[5] Benedict and Talbot,[6] Murlin and Hoobler,[7] Bailey and Murlin[8] and others,* all of these observers paying especial attention to the question of muscular activity. On account of the difficulty of keeping infants quiet, Benedict and Talbot, and Murlin, Hoobler and Bailey were obliged to feed most of their subjects shortly before the experiment was started. It is quite possible that a lowering of metabolism during sleep may have counterbalanced the slight increase due to the milk ingestion.

All of the above investigators have thrown new light on the subject. It would too greatly extend the bounds of this article to discuss in detail the several excellencies contained in their work. Of special interest is the fact that the metabolism of babies in the first month of life is

3. Magnus-Levy and Falk: Der Lungengaswechsel des Menschen in verschiedenen Alterstufen, Arch. f. Anat. u. Physiol., 1899, Suppl. 315.

4. Howland: Der Chemismus und Energieumsatz bei schlafenden Kindern, Ztschr. f. physiol. Chem., 1911, lxxiv, 1.

5. Schlossman and Murschauser: For references see note 6.

6. Benedict and Talbot: The Gaseous Metabolism of Infants, Carnegie Institution of Washington, Pub. 201, 1914; Studies in the Respiratory Exchange of Infants, Am. Jour. Dis. Child., 1914, viii, 1.

7. Murlin and Hoobler: The Energy Metabolism of Ten Hospital Children, Am. Jour. Dis. Child., 1915, ix, 81.

8. Bailey and Murlin: The Energy Requirement of the New-Born, Am. Jour. Obst., 1915, lxxi, 1.

* Just as this article is going to press Dr. Benedict has kindly called attention to the following reference: Olin: Carbon Dioxid Production in Boys of from 10 to 18 Years of Age; Finska Läksällsk: Handl Helsingfors, 1915, lvii, 1434.

very low. This was apparently first discovered by Hasselbach,[9] and later independently by Murlin,[7] who first brought it to general attention. The same point was shown in Table 7 of Paper 4 of this series.

The metabolism of normal adults has been thoroughly studied in the last few years. Benedict, Emmes, Roth and Smith[10] have collected 157 subjects, some of them as young as 15 years, using chiefly the Benedict universal respiration apparatus. Palmer, Means and Gamble,[11] with the same instrument, have collected a considerable number of normal records and Means[12] has recently calculated his results according to measurements taken by the new surface area formula described in Paper 5[13] of this series. We have also at our command the normal controls of Paper 4[14] and those of Papers 11 and 13, studied in the Sage calorimeter.

All of the above mentioned work on adults was done with very quiet subjects twelve or more hours after the last meal, and the technic of the observers was almost exactly the same. The results of these experiments have been charted in the accompanying curves, together with the work of Magnus-Levy and Falk, of Howland, Benedict and Talbot, Murlin and Hoobler, and Bailey and Murlin for comparison with the new results obtained on the boys 12 and 13 years old. Many other careful workers have studied the normal metabolism, but it has seemed best to use only the above mentioned investigations.

METHOD OF EXPERIMENTS

The Sage calorimeter and the methods employed in this research have been fully described in the previous papers of the series entitled Clinical Calorimetry.[15] The surface area of the boys was determined according to the so-called "Linear Formula" described in Papers 5, 9 and 10. The calories derived from protein were calculated from speci-

9. Hasselbach: Respirations—For søg Paa Nyfødte Dørn, Bibliot. f. Læger, 1904, 8 de Række 5th Bind, 219.

10. Benedict, Emmes, Roth and Smith: The Basal, Gaseous Metabolism of Normal Men and Women, Jour. Biol Chem., 1914, xviii, 139. Benedict and Roth: The Metabolism of Vegetarians as Compared with the Metabolism of Non-Vegetarians of Like Weight and Height, Ibid, 1915, xx, 231. Benedict and Smith: The Metabolism of Athletes as Compared with Normal Individuals of Similar Height and Weight, Ibid, p. 243. Benedict and Emmes: A Comparison of the Basal Metabolism of Normal Men and Women, Ibid, p. 253. Benedict: Factors Affecting Basal Metabolism, Ibid, p. 263.

11. Palmer, Means and Gamble: Basal Metabolism and Creatinin Elimination, Jour. Biol. Chem., 1914, xix, 239.

12. Means: Basal Metabolism and Body Surface, Jour. Biol. Chem., 1915, xxi, 263.

13. Clinical Calorimetry, Paper 5, The Archives Int. Med., 1915, xv. 868, 870.

14. Clinical Calorimetry, Paper 4, The Archives Int. Med., 1915, xv, 835.

15. Papers 1 to 8, The Archives Int. Med., 1915, xv, 793-945; Papers 9 to 17, Ibid., 1916, xvii, 855-1059.

TABLE 1.—Results of Calorimeter—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
F. R. S.	Prelim.	10:57	.....	.....	.....	.....	.....	.....	.....
3/20/15									
32.09 Kg.	1	11:57	19.62	17.43	0.819	28.29	0.458	57.95	63.13
1.124 Sq. M.	2	12:57	19.41	16.98	0.831	27.91	0.458	56.65	59.22
	3	1:57	21.10	18.32	0.838	30.54	0.458	61.33	63.38
								175.93	
J. D. D. B.	Prelim.	11:01	.....	.....	.....	.....	.....	.....	.....
3/26/15									
34.52 Kg.	1	12:01	19.21	15.60	0.896	25.33	0.510	52.72	59.65
1.224 Sq. M.	2	1:01	19.39	17.89	0.789	25.89	0.510	58.92	64.52
								111.64	
Raymond M.	Prelim.	11:14	.....	.....	.....	.....	.....	.....	.....
4/3/15									
30.41 Kg.	1	12:14	19.46	17.04	0.830	25.47	0.390	56.99	55.38
1.084 Sq. M.	2	1:14	19.81	18.40	0.783	26.35	0.390	60.96	55.90
								117.95	
Reg. F.	Prelim.	11:01	.....	.....	.....	.....	.....	.....	.....
4/5/15									
35.44 Kg.	1	12:01	21.07	16.87	0.908	26.85	0.411	57.55	65.26
1.22 Sq. M.	2	1:06	25.87	19.37	0.971	29.66	0.411	66.13	73.41
								123.68	
Harry B.	Prelim.	11:05	.....	.....	.....	.....	.....	.....	.....
4/6/15									
36.57 Kg.	1	12:05	20.97	17.85	0.854	33.11	0.594	59.66	62.59
1.232 Sq. M.	2	1:05	20.48	17.03	0.875	32.13	0.594	57.15	62.87
								116.81	
Henry K.	Prelim.	11:10	.....	.....	.....	.....	.....	.....	.....
4/7/15									
35.98 Kg.	1	12:10	20.24	16.38	0.898	26.17	0.251	55.94	60.17
1.224 Sq. M.	2	1:10	21.55	18.87	0.831	28.67	0.251	63.39	64.75
								119.33	
Arthur A.	Prelim.	11:13	.....	.....	.....	.....	.....	.....	.....
4/8 15									
30.59 Kg.	1	12:13	17.57	17.01	0.751	21.74	0.308	55.84	59.51
1.126 Sq. M.	2	1:13	18.64	16.97	0.799	21.58	0.308	56.46	58.32
								112.30	
Leslie B.	Prelim.	11:15	.....	.....	.....	.....	.....	.....	.....
4/9 15									
28.53 Kg.	1	12:15	19.81	18.16	0.793	24.21	0.437	60.08	56.12
1.050 Sq. M.	2	1:15	16.87	14.40	0.852	21.17	0.437	48.21	47.50
								108.29	

—Experiments on Boys

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
.....	37.24	..	..	....	..	..	..	.....	.....	Basal
58.79	37.09	81	15	0.82	21	48	31	1.806	46.62	
59.80	37.11	78	24	0.84	21	43	36	1.765	45.58	
63.30	37.13	80	34	0.85	20	41	39	1.911	49.34	Restless. Excluded from basal averages
181.89										
.....	37.56	..	..	....	..	..	..	.....	.....	Basal
55.27	37.42	78	7	0.93	18	26	56	1.527	40.40	
61.02	37.32	76	16	0.78	23	58	19	1.707	45.15	
116.29										
.....	36.83	..	..	....	..	..	..	.....	.....	Basal
54.63	36.90	83	5	0.84	18	45	37	1.874	47.49	
56.54	37.21	87	12	0.78	17	62	21	2.005	50.80	
111.17										
.....	37.35	..	..	....	..	.	..	.....	.....	Basal
55.34	37.10	78	5	0.94	19	17	64	1.624	43.34	
69.40	36.99	80	20	1.01	17	0	83	1.866	49.80	
124.74										
.....	37.30	..	..	....	..	.	..	.....	.....	Basal
59.03	37.18	88	5	0.87	26	33	41	1.632	43.97	
61.19	37.15	89	5	0.90	28	25	47	1.563	42.12	
120.22										
.....	37.02	..	..	....	..	..	..	.....	.....	Basal
51.77	36.74	88	5	0.91	12	27	61	1.555	41.65	
67.20	36.83	87	7	0.83	11	52	37	1.762	47.20	
118.97										
.....	36.89	..	..	....	..	..	..	.....	.....	Basal
54.24	36.69	81	11	0.74	15	75	10	1.825	46.38	
58.88	36.72	82	4	0.80	14	58	28	1.846	46.89	
113.12										
.....	37.46	..	..	....	..	..	..	.....	.....	Basal
55.40	37.44	..	10	0.79	19	58	23	2.106	52.24	
44.53	37.33	88	5	0.87	24	34	42	1.690	41.92	
99.93										

mens voided between the hours of 9 a. m. and 1:15 p. m. Twenty-four-hour specimens could not be secured.

The subjects of the experiments here discussed were all healthy, normal boys between their twelfth and fourteenth birthdays. Two of them, F. R. S. and J. D. D. B., were related to members of the calorimeter staff, the others were Boy Scouts from one of the suburbs. A month or so before the research had been planned the writer had given the required physical examination to a group of sixteen Boy Scouts. The scout master selected as subjects for the experiments the five who most needed to earn money for uniforms. Harry B. was chosen because he was a patrol leader and able to manage the other boys. All the eight boys lived in the suburbs except J. D. D. B., who was home on a vacation from boarding school. They were all bright mentally and active physically, apparently being in constant motion when not studying or sleeping. The urine was examined in all cases and found to be normal.

In order to accustom the boys to the apparatus, they were brought to the calorimeter room a week or so before the experiment, sealed in the apparatus for a short time and trained in the simple routine. This was omitted in the case of F. R. S., who had helped his father build parts of the machine and was thoroughly familiar with the work. All of the boys considered the adventure as a lark and not one was apprehensive. A small breakfast, consisting of an egg, a slice of toast and a glass of milk, was allowed them at 7 o'clock, because it seemed probable that boys of this age would be ravenous and irritable if sent in from the country in a fasting condition.

The problem of keeping the youngsters quiet for three hours was hard to solve. It seemed best to allow them to read for one of the hours in a small book with large print. This proved satisfactory, the work involved in holding the book and turning the pages was very small. During the rest of the time the boys were bored. F. R. S. and J. D. D. B. remained quiet for two hours, but the former was so restless in the third period that experiments of this length were not attempted again. For the six Boy Scouts another expedient was tried. All the boys were anxious to earn pocket money and all were liberally paid for the experiments. A system of fines was instituted and the boys were told that one cent would be withheld for each centimeter that the work-adder tallied above 15 per hour. This figure was arbitrarily selected since it represents the average activity of a quiet subject who turns over once or twice an hour and shifts his position a few times to make himself comfortable. The boys took good care not to approach the danger mark. After the fine system was started the 15 centimeter mark was exceeded in only one period, and the lads as a group were the quietest of subjects.

TABLE 2.—Summary of Experiments on Boys

Name	Age		Weight, Kg.	Height, Cm.	Circumference of Thorax, Cm.	Signs Approaching Puberty	Surface Area, Sq. Meters		Calories per Kg. per Hr.	Meeh's Formula		Linear Formula		Average R. Q.	Average Pulse
	Years	Mos.					Meeh's Formula	Linear Formula		Calories per Sq. Meter per Hr.	Per Cent. above Adult Aver., 34.7	Calories per Sq. Meter per Hr.	Per Cent. above Adult Aver., 39.7		
J. D. D. B.	12	2	34.52	152.8	67.3	+	1.305	1.224	1.62	42.8	23	45.6	15	0.84	77
Leslie B.	13	3	28.53	140.8	61.8	±	1.150	1.050	1.90	47.1	36	51.6	30	0.82	88
Raymond M.	12	7	30.41	140.5	65.8	0	1.200	1.084	1.94	49.1	42	54.4	37	0.81	85
Reginald F.	12	8	35.44	148.2	68.2	+	1.328	1.220	1.75	46.6	34	50.7	28	0.94	79
F. R. S.	12	10	32.09	141.5	66.2	0	1.243	1.124	1.79	46.1	33	51.0	29	0.83	80
Arthur A.	13	8	30.59	146.6	65.4	0	1.204	1.126	1.84	46.6	33	49.9	26	0.78	81
Harry B.	13	10	36.57	146.0	71.4	+ +	1.357	1.232	1.60	43.0	24	47.4	19	0.86	88
Henry K.	13	11	35.98	148.2	67.7	±	1.343	1.224	1.66	44.4	28	48.8	23	0.86	87
Average	..	..	.....	.....	....	..	.....	.....	1.70	45.7	32	49.9	26	0.84	83

The question may be raised as to whether or not the breakfast taken by the subjects between 7 and 7:30 a. m. increased the metabolism between the hours of 11 and 1 o'clock. The standard meal allowed consisted of 1 egg, 1 glass of milk and 1 slice of toast with butter. They were shown standard portions of these and copied them as closely as possible, except Arthur A., who took nothing but 1 egg. The meal contained approximately 17 gm. of protein, 22 of fat and 30 of carbohydrate, with about enough calories to maintain a boy 5½ hours, if we allow an increase of 20 per cent. over the basal metabolism, to cover the journey to the hospital. J. D. D. B., who took his breakfast half an hour later than the others, had the lowest metabolism and Arthur A., who took the smallest breakfast, had almost the highest heat production. Mr. H. L. Higgins of the Nutrition Laboratory in Boston, kindly made a series of observations on a young man who took this same breakfast and found that the metabolism returned to its fasting level 3½ hours after the meal. It may perhaps be said that the metabolism was increased by the ride of fifty minutes in the train, ten minutes in the street cars and the walk of five minutes. The boys all reached the hospital by ten minutes past 9, sat in a chair for three fourths of an hour, undressed and lay on the bed within the calorimeter at about 10 o'clock, the experiment beginning at 11, or three and one half to four hours after breakfast. It will be noted that there was no significant drop in pulse rate or metabolism in the second periods. It is exceedingly doubtful if the combined increase due to the previous exercise, the specific dynamic action of food and the quiet reading amounted to 5 per cent. above the fasting level at absolute rest.

DESCRIPTION OF SUBJECTS

F. R. S., 12 years and 10 months old. He has been perfectly well except for one attack of abdominal pain in 1911, diagnosed as appendicitis.

Physical Examination.—Short, muscular and unusually well built; no signs of approaching puberty; disposition very active.

This boy was the son of the laboratory technician, who built and still operates the calorimeter, and he was thoroughly at home in his surroundings, having in fact helped to make the bed on which he lay. He was the only boy placed in the calorimeter for an experiment without previously staying for a short period in the apparatus. On the morning of the observation he took the standard breakfast at 6:40 a. m. While in the calorimeter he read quietly for the first hour. In the second hour he tried to sleep and was somewhat restless for part of the time. In the third hour he read for five minutes, and during the remainder of the time was so restless that this period has been excluded from the averages.

J. D. D. B., aged 12 years, 2 months. In 1911 he had measles; about six months prior to the experiment he suffered from a number of furuncles in the outer ear, and two weeks before the experiment had a cold in the head which lasted four days.

Physical Examination.—Very tall for his age, complexion dark, bones long and not heavy, very little subcutaneous fat, muscles sinewy; temperament rather

high-strung but under good control; genitalia just beginning to develop; there were a few pubic hairs; voice not yet affected.

On the morning of the experiment he took the standard breakfast at 7:45 a. m., and came to the hospital in the street cars, being the only boy who lived in the city. In the first hour he was almost motionless and slept for a short time, and in the second period he read quietly in a small book.

Raymond M., aged 12 years, 7 months. He remembers that he had whooping cough as a baby and that he had measles two years previous to the experiment. He is short, stocky and muscular, but the thorax is rather narrow with a prominent sternum. His complexion is light and his disposition quiet. His physical examination is normal except that the right tonsil is moderately enlarged. He shows no signs of approaching puberty.

On the morning of the experiment he took the standard breakfast at 7:30 a. m. During the first period he read very quietly and in the second period tried to sleep.

Reginald F., aged 12 years, 8 months. He remembers no illnesses except measles; he is tall, slim, of graceful build; his hair is brown; the pubic hair is just making its appearance and his voice suggests slight change; both mammary glands are palpable, measuring about 10 by 2 mm. The left gland is slightly tender.

Standard breakfast at 7:15 a. m. In the first period he was very quiet, reading for twenty minutes. In the second period he slept for twenty minutes but was restless during the remainder of the time.

Harry B., aged 13 years, 10 months. Born in England; has been in this country eleven years; had measles in childhood and two weeks before the experiment was sick in bed a couple of days with stomachache. The day before he noticed a slight infection of his finger which pained him until it discharged a little pus. On the day of the experiment it did not hurt and he felt perfectly well.

Physical Examination.—Of moderate height and stocky muscular build, with broad shoulders; complexion fair. The left forefinger is red and slightly swollen near the nail, but there is no redness up the arm and no tenderness or swelling of the axillary nodes. The genitalia are approaching the adult type in development and there is a scant growth of pubic hair, and the mammmary glands are just palpable. The voice has not yet started to change.

He took the standard breakfast at 7:15 a. m. During the first hour he was awake but very quiet, and in the second hour he was also quiet, reading for thirty minutes.

Henry K., aged 13 years 11 months. Does not remember any illnesses except measles. He is tall, fairly muscular and well built except for the chest, which is narrow, with a prominent sternum. The upper jaw is narrow with high arch and prominent incisor teeth. His complexion is fair, his disposition quiet. The only sign of approaching puberty is a scant growth of pubic hair.

He ate the standard breakfast at 7 a. m. In the first hour of the experiment he was practically motionless and in the second hour was very quiet, reading for fifty minutes.

Arthur A., aged 13 years, 8 months. Thinks he had measles and mumps when 3 or 4 years of age; three years prior to the experiment he broke his femur in a coasting accident. There is now no shortening of the limb. He is of slight, sinewy build with well formed chest, but gives the impression of being somewhat undernourished; complexion fair, disposition rather nervous; no signs of approaching puberty.

The evening before the experiment he was taken, with the other Boy Scouts, to an exhibition drill and in the excitement took no supper except one bun at 5 p. m. On the morning of the observation in the calorimeter he ate nothing but an egg at 7 a. m. He was very quiet both hours, reading forty minutes in the second period.

Leslie B., brother of Harry B., aged 12 years, 3 months. In childhood he had measles and chickenpox. For the last few months he has had no appetite for breakfast and had suffered from stomachaches. He is of small frame, rather thin and undernourished but his color is good and his muscles strong. His complexion is fair and his disposition bashful and quiet. His teeth are in poor condition and his tonsils are enlarged. In the abdomen several masses of constipated feces are palpable. The only sign of approaching puberty is a scant growth of pubic hair.

On the morning of the experiment he took the standard breakfast at 7 a. m. In the first period he was quiet, reading for forty-five minutes. In the second period he was unusually quiet, sleeping about three-quarters of the time. He was perfectly well until he came out of the calorimeter. He then felt faint, but recovered quickly.

DISCUSSION OF RESULTS

The total heat production in the eight experiments as measured by the method of indirect calorimetry was 985.93 calories, by the method of direct calorimetry 986.33 calories, a difference of 0.04 per cent.

A summary of the results obtained on the boys will be found in Table 2. It will be noted that the metabolism averaged 32 per cent. above the adult figure per unit of surface area according to Meeh's formula, or 25 per cent. above according to linear figure. The true significance of these results can be appreciated only if we consider the variations in the intensity of metabolism from birth to old age. It is for this reason that the results on normal individuals have been grouped in Charts 1 to 3. The first (Chart 1) represents the metabolism from birth to the age of 24 calculated per *kilogram of body weight*. It will be noted in general that the heat production of the infants shows wide variations, but at a much higher level than that of the adults. A uniform decrease in the metabolism becomes evident after the sixth year, becoming less marked after the twentieth year. In Paper 4 of this series we have mentioned the disadvantages of using the body weight as a basis of comparison of individuals of different sizes. Small animals show per kilogram a calorific production so much greater than that of large animals that it is almost a waste of time to compare children and adults by using this standard. For clinical purposes, however, the body weight is a convenient guide.

Chart 2 shows the metabolism from birth to the age of 24 expressed in terms of calories per square meter of body surface as determined by Meeh's formula. Lines have been drawn showing as nearly as possible the averages for males and females. It will be seen that the metabolism is low at birth, increases rapidly during the first year, reaches its maximum in the almost unexplored period between the ages of 1 and 6, falls quite rapidly until the age of 20, then very slowly. During infancy there is no apparent difference between the sexes, but after the age of 6 the girls and women have a distinctly lower metabolism.

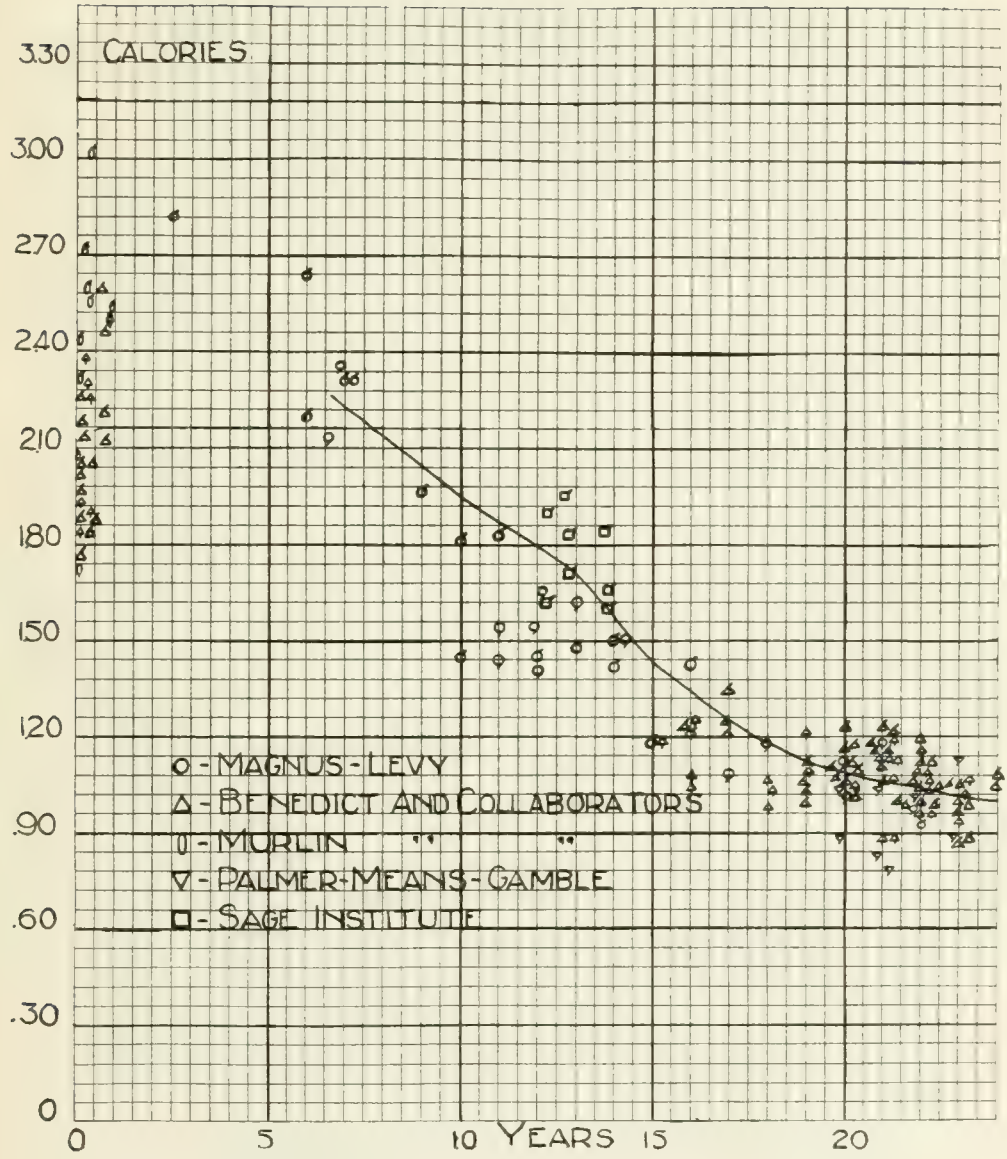
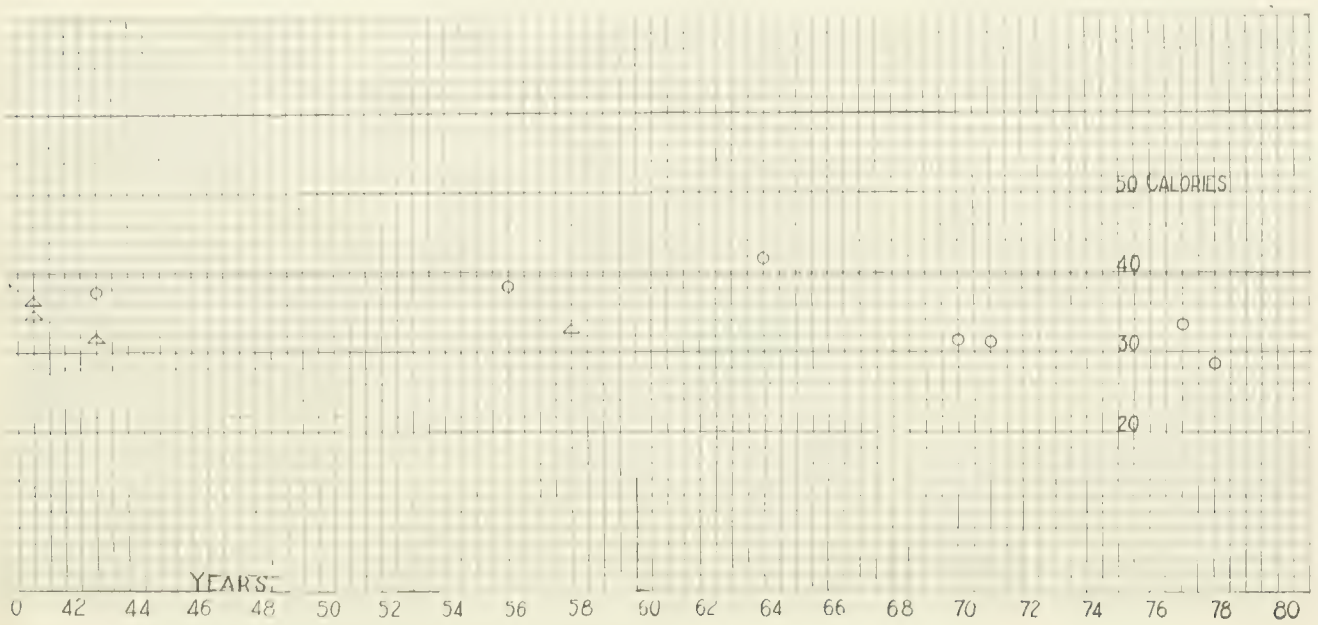


Chart 1.—Variation of basal metabolism with age: Calories per hour per kilogram of body weight.

In Papers 4 and 5 we have shown the reasons for preferring the calories per unit of surface area as a guide for the intensity of the metabolism, and have also shown the errors and limitations of Meeh's formula which has been the standard for so many years. The fact that the formula shows an average plus error of 16 per cent. scarcely affects its value for purposes of comparison with subjects of usual build. On the other hand, the tendency of this error to be much smaller in the case of thin subjects and larger in the case of fat ones, is of considerable importance. New-born infants are relatively thin, older children relatively chubby until the age of 4 or 5, when they grow taller and thinner until puberty. Women tend to put on weight after 30 and men do so five or ten years later. If, therefore, we try to correct the curve for these errors in Meeh's formula we find that the peak in early childhood will be accentuated and the rest of the curve flattened out.

Chart 3 gives the results for males expressed in terms of calories per square meter of body surface as determined by the new so-called "Linear Formula." It will be seen that the metabolism of the adults is somewhat more uniform and that the boys average only 25 per cent. above the adult level instead of 32 per cent. as in the previous chart. This indicates a true increase of 25 per cent. above the heat production which a group of normal adults would show if they were the same size as the boys. For purposes of comparison the metabolism of the infants has been recorded in terms of Lissauer's Formula.[13]

When we consider the question of the metabolism in the first year or so of life we must remember that the infant differs greatly from the adult in the proportions of the body and the relative size of the various organs. A baby 5½ feet tall would be a short legged, long bodied monster with an enormous head. He would have a very large liver and a comparatively large thyroid gland. At birth the liver comprises 4.5 per cent. of the body weight and during adult life less than 3 per cent. Since this is supposed to be a gland of high metabolic activity, one would naturally expect an increased heat production in an organism with a relatively large liver. Still more important in regulating metabolism is the thyroid gland, which is considered to be three times as large in the new-born as in the adult, although recent measurements by Parski makes the figures somewhat smaller. Thyroid secretion has such a marked effect on development that it is quite possible that the gland is relatively more active in childhood. Some might even argue that the increased metabolism of this period is in itself evidence of a greater activity of the thyroid. Such a theory would be unwarranted unless supported by a greater number of facts than are now available. It should be remembered that the phenomena of growth are not so very different with invertebrates which have no thyroids.



per hour per square meter of body surface. Linear formula.

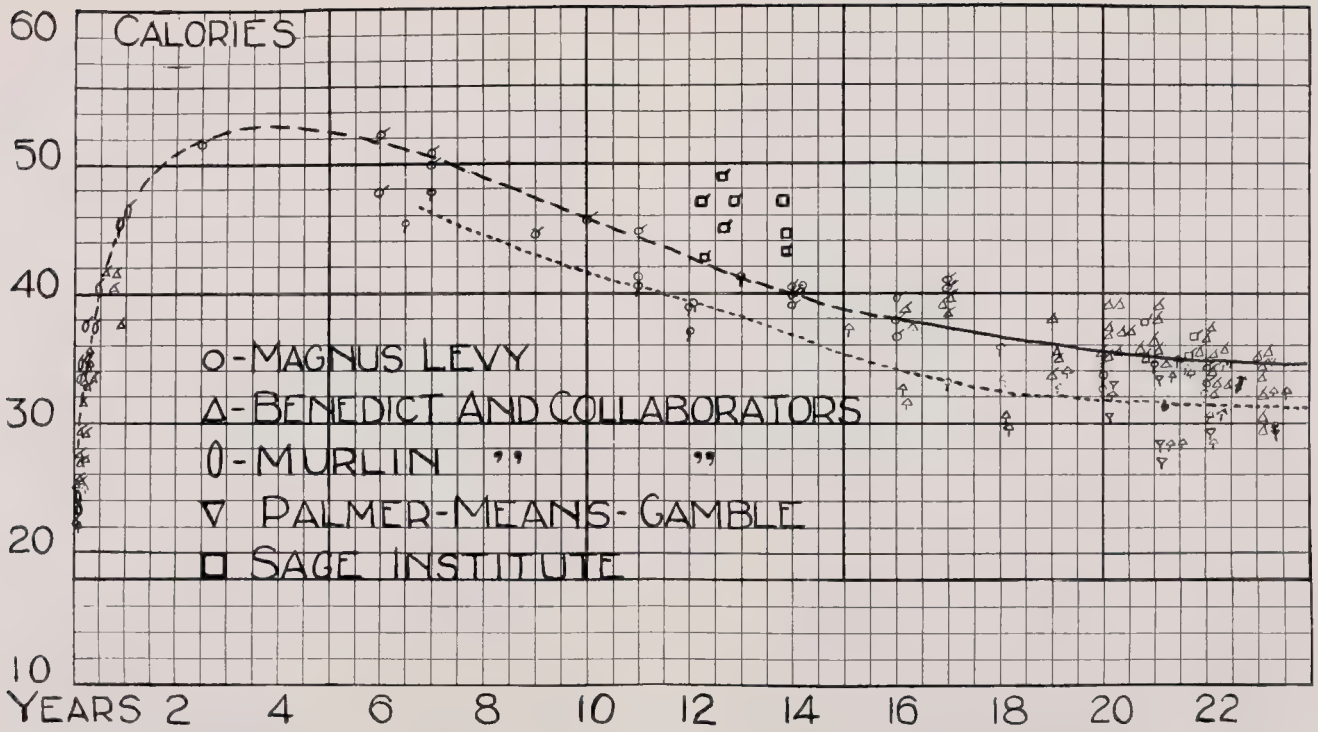


Chart 2.—Variations of basal metabolism with age: Calories per hour per square meter of body surface—Meeh's formula. Dash line shows average for males, dotted line for females

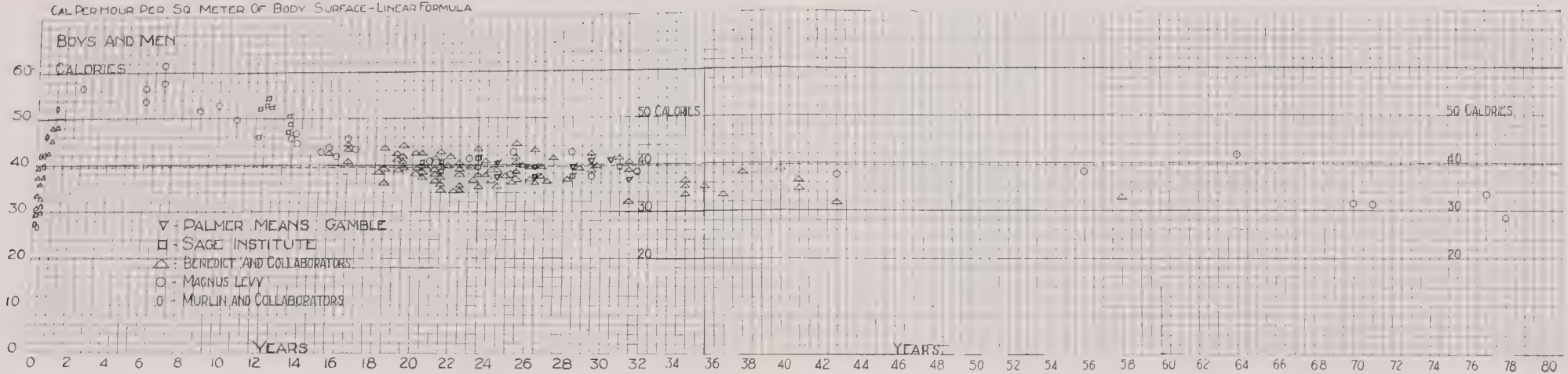


Chart 3.—Variation of basal metabolism with age; Calories per hour per square meter of body surface- Linear formula.

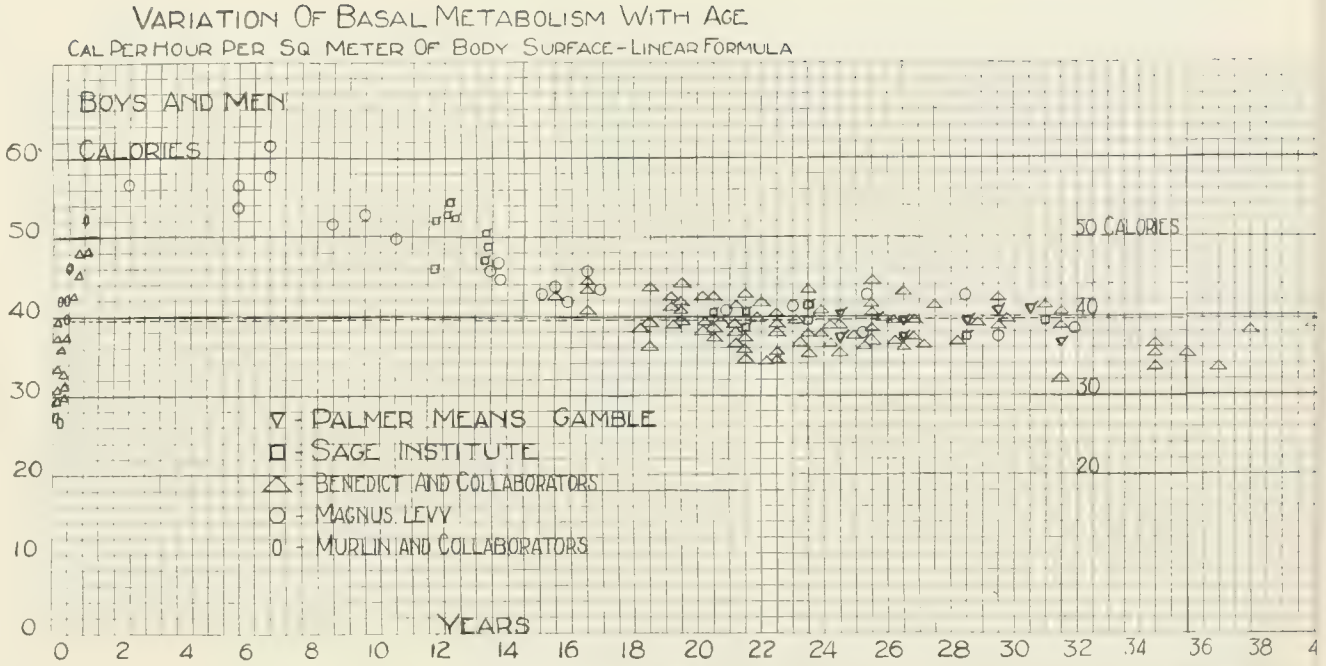


Chart 3.—Variation of basal metabolism with age; Calories

The Sage calorimeter has recently been able to throw an interesting sidelight on the relationship of body form to metabolism. Two men who in youth had lost both legs in accidents, were studied in the respiration chamber and the surface area determined by formula and actual measurement. The one who was fat showed a metabolism only 4 per cent. above the normal average; the one who was muscular was 2 or 3 per cent. above. These men resembled infants in the relative proportion of body to extremities. This indicates that the law of surface area holds true under dissimilar physiological conditions such as are found in legless men. The high metabolism of infants is not therefore, due to the differences in body shape and body composition.

These factors are almost entirely ruled out in the case of the boys 12 and 13 years old. At this age the body has assumed almost the adult proportions and the liver and thyroid are not much larger in proportion to the body weight than in later life. The metabolism of these boys is very much higher than that of adults. It is rather a striking fact that the metabolism was distinctly higher in the boys who showed no signs of approaching puberty than in those who showed traces of pubic hair and increasing development of the genitalia. It is hoped that the same group of boys can be studied at intervals during pubescence. These boys can be compared with the case of infantilism studied by McCrudden and Lusk in the calorimeter of the Department of Physiology of the Cornell Medical College. This dwarf, who was 17 years old, and about the size of an average boy of 6 years, showed a metabolism of 23.3 calories per hour per square meter (Meeh), which was 7 per cent. below the adult normal average.

The growth of children in length and weight is very rapid during the first two years of life and then decreases somewhat between the ages of 8 and 12. Following this is a period of increased growth, with relatively greater gain in stature than in weight. This begins in almost all the nations at the age of 12 or 13 in boys and reaches its height between the thirteenth and fifteenth years. The figures of Boas[16] and Burk[17] are well worth consulting, and Wiener's[18] measurements of three of his sons show this increase in the period of prepubescence very clearly. The curve of weight is somewhat different, since boys become relatively thinner as they grow tall and do not fill out again

16. Boas: The Growth of Toronto Children, Report U. S. Commr. Education, 1896-97, ii, 1541.

17. Burk: Growth of Children in Height and Weight, Am. Jour. Psychol., 1898, ix, 253.

18. Wiener: Das Wachstum des menschlichen Körpers, Karlsruhe, 1890. Chart reproduced in Burk's paper (note 17) and also in Hall's Adolescence, New York, 1904.

until puberty is well established. In the case of girls the period of increasing growth comes a year or two earlier.

In adult life the nearest approach to the growth of childhood is found in the period of convalescence from acute infectious diseases. The fact that the metabolism is increased at such times was demonstrated by Svenson, Rolly and others. Coleman and Du Bois[19] have shown that after typhoid the metabolism which falls to normal at the end of the fever, may rise to an average of 17 per cent. above normal in the second and third weeks of convalescence. It is significant that the body which is repairing the losses of protein and fat during the fever should be maintaining its metabolism at a level which approaches that found in childhood. It is also significant that a second peak in the curve representing the heat production at different ages is found in the case of these boys just at the period of a renewed increase in the rate of growth. The evidence points toward a specific increase in the metabolism of the growing organism.

There is no apparent explanation for the fact that the metabolism was higher in the boys who showed no signs of approaching puberty than in the others. It is difficult to explain the low metabolism of newborn infants. It must be considered, however, that the unborn baby is essentially similar to an internal organ which is practically free from the play of external physical stimuli. Under such conditions the heat production must be on a different level from that in later life after a fuller development of the neuromuscular elements has been completed.

SUMMARY AND CONCLUSIONS

Eight normal boys, 12 or 13 years old, were studied in the respiration calorimeter four to six hours after a small breakfast. They were allowed to read for one of the two experimental hours, but were very quiet. The methods of direct and indirect calorimetry agreed within 0.04 per cent. Their heat production per unit of surface area was 32 per cent. higher than the adult level according to Meeh's formula, or 25 per cent. higher according to the more accurate "Linear Formula."

In studying the effect of growth on metabolism, interpretation of the results obtained on infants is complicated by the fact that babies differ greatly from adults in the proportions of the body and the relative size of the viscera, notably the liver and thyroid. Boys just before the onset of puberty have almost adult proportions. They are in the midst

19. Coleman and Du Bois: The Influence of the High Calory Diet on the Respiratory Exchanges in Typhoid Fever, THE ARCHIVES INT. MED., 1914, xiv., 168; also Clinical Calorimetry, Paper 7, ibid., 1915, xv., 887.

of a period of accelerated growth. The fact that the metabolism is high, points to a specific increase in the metabolism of the growing organism.

The writer wishes to thank those whose assistance made this research possible. The electrical measurements were made by Mr. F. G. Soderstrom, the residual analyses and calculations by Dr. A. L. Meyer and the calculations were checked by Miss Grace Sims. Urinalyses were made by Mr. F. C. Gephart and Mr. R. H. Stone.

CLINICAL CALORIMETRY

THIRTEENTH PAPER

THE BASAL METABOLISM OF NORMAL ADULTS WITH SPECIAL REFERENCE TO SURFACE AREA*

FRANK C. GEPHART, A.B., AND EUGENE F. DU BOIS, M.D.
NEW YORK

Since the writing of Paper 4[1] of this series an unusual amount of work has been published on the subject of the normal metabolism. It is now possible to calculate the normal baseline much more exactly than a year ago and it is therefore necessary to reconsider the whole question at this early date. The figures representing the average normal metabolism have been changed frequently since the study of the respiratory exchanges began and it may be said that the chief advance has depended on the fact that it has been possible to make the variation in the normal smaller and smaller each year. With the oldest type of large respiration chamber the range of heat production fluctuated enormously with the uncontrolled influences of muscular activity and the specific dynamic action of food. With the improved technic of Johansson and with the small apparatus of the Zuntz school these factors were eliminated, but errors due to changes in the calorific factors for O_2 and CO_2 remained. The normal variation was frequently quoted as from about 2.5 to 5.0 c.c. O_2 per kilogram and minute with a mean of about 3.5 c.c. Under these conditions a pathological departure from the average normal as great as 40 per cent. might be obscured. In 1914 Coleman and Du Bois[2] gathered 48 controls from various sources including seven studied in the Sage calorimeter and gave the figure 34.2 calories per hour as the average heat production per square meter of body surface as determined by Meeh's formula. They pointed out that the normal variation was only plus or minus 10 per cent. if the surface area were used as a standard. In Paper 4 of this series,[1] on the basis of a much larger number of controls, we selected the average

* Submitted for Publication Feb. 4, 1916.

* From the Russell Sage Institute of Pathology, in affiliation with the Second Medical Division of Bellevue Hospital.

1. Gephart and Du Bois: Clinical Calorimetry, Paper 4, THE ARCHIVES INT. MED., 1915, xv, 835

2. Coleman and Du Bois: The Influence of the High Calory Diet on the Respiratory Exchanges in Typhoid Fever, THE ARCHIVES INT. MED., 1914, xiv, 168.

figure of 34.7. Since then Benedict, Emmes, Roth, and Smith[3] have published the details and have discussed their experiments which were only briefly reported at the time of our last publication. They found the metabolism of vegetarians to be practically the same as that of nonvegetarians, while the athletes average 7 per cent. higher than the nonathletes used as controls. This is accounted for in part by the fact that the athletes were somewhat younger than the controls with whom they were compared. The average age of the fifteen athletes was 22⅓ years and the average heat production 40.7 calories per square meter per hour as recalculated according to the height-weight chart. This is only 2.5 per cent. higher than our standard for normal men. Benedict and his co-workers have pointed out the fact that the younger subjects show a higher metabolism and that the heat production is much lower when the subject is asleep at night than when he is awake in the day time. They have found the metabolism of women average about 6 per cent. lower than that of men. The extremes of variation in the oxygen consumption of the same man over the course of months and years are shown in a very instructive table of thirty-five subjects. Eleven show a variation less than 10 per cent., eighteen show from 10 to 20 per cent. and six a difference of 20 to 31 per cent., the average variation being 13.9 per cent. It must be remembered that this table shows the extremes, giving the percentage increase of the very highest period over the very lowest. The results in an early morning period when the subject was asleep may be contrasted with an afternoon period when he was awake and weary of experimentation. The "Universal" respiration apparatus with which these tests were made can be used only for periods of 10 to 20 minutes and with some people there may be a considerable amount of discomfort from the mouth or nose pieces. On the whole it is quite remarkable that the extremes of variation are not greater. It is to be hoped that the details of this table will be published so that we may estimate the frequency with which observations under similar conditions show results which differ materially from the average. Benedict also calls attention to the variation of the metabolism of different individuals according to body weight and surface area.

Palmer, Means and Gamble[4] have studied a considerable number of normal men and women and have found that the creatinin elimination bears a constant relationship to the basal heat production. Means[5] has

3. Benedict, Emmes, Roth and Smith: Jour. Biol. Chem., 1914, xviii, 139. Benedict and Roth: The Metabolism of Vegetarians as Compared with the Metabolism of Non-Vegetarians of Like Weight and Height, ibid, 1915, xx, 231. Benedict and Emmmes: A Comparison of the Basal Metabolism of Normal Men and Women, ibid, xx, p. 253. Benedict and Smith: The Metabolism of Athletes as Compared with Normal Individuals of Similar Height and Weight, ibid., xx, p. 243. Benedict: Factors Affecting Basal Metabolism, ibid, xx, p. 265.

4. Palmer, Means and Gamble: The Basal Metabolism and Creatinin Elimination, Jour. Biol. Chem., 1914, xix, 239.

5. Means: Basal Metabolism and Body Surface, ibid, 1915, xxi, 263.

calculated out the metabolism of these same subjects according to square meters of body surface as determined by Meeh's formula and by the new linear formula described in Paper 5 of this series. The average figure for men according to Meeh's formula was 33.2 calories per hour, according to the "Linear Formula" 39.6. The averages for women were lower, Meeh's formula 29.9, "Linear Formula" 38.2. The greatest variation from the average was 12.3 per cent. according to Meeh's formula and 7.9 per cent. according to the linear, the mean variations were 4.8 per cent and 4 per cent., respectively. Means[6] has also shown that the apparent depression of metabolism in obesity in most cases was due to the large plus error in Meeh's formula, and that according to the linear formula his two very stout subjects came within normal limits.

In Papers 5 and 9 in this series attention has been called to the variable plus error in Meeh's formula, which averages about 15 per cent., and a formula based on linear measurements has been described. In Paper 10 a "Height-Weight" formula is given which makes it possible to determine the approximate surface area of subjects described in publications in which the height and weight are stated. Results expressed in terms of square meters of surface area are comparable if either the linear formula or "Height-Weight Formula" be used, but are about 15 per cent. higher than if Meeh's formula be applied. This necessitates the use of two different sets of figures to represent the average metabolism of men between the ages of 20 and 50—39.7 calories per square meter per hour according to the linear formula, 34.7 calories according to Meeh's formula. In Paper 11 it is shown that the metabolism is slightly lower in the semireclining posture than flat in bed. In Paper 12 the increase in metabolism during the period of growth is discussed in detail.

METHODS AND SUBJECTS

The methods described in Paper 4 of this series were followed in the present work. Many of the subjects have been reported in previous papers.

Morris S., former typhoid patient, is reported in Paper 6 where the history and experimental data are given. At the date of the experiments here discussed he was in perfect health. Dec. 17, 1914, a basal determination was made and the next day between 8:40 and 9:20 a. m. he ate the protein meal, consisting of 110 gm. egg white, 21 gm. egg yolk, 600 c.c. fat-free milk, 150 gm. pot cheese and 10 gm. lactose. This according to analysis of the cheese and milk contained 9.6 gm. nitrogen. He was quiet throughout the experiment and during the third hour slept for forty minutes. The metabolism was much lower during this hour and it should be excluded from the averages.

Albert G. Normal control whose history is given in Paper 12. Dec. 30, 1914, he was given 79 gm. olive oil at 10:15 a.m. During the first and second periods

6. Means: Studies of the Basal Metabolism in Obesity and Pituitary Disease, Jour. Med. Research, 1915, xxvii, 121.

he slept fourteen and ten minutes, respectively. Jan. 4, 1915, at 10:13 a.m. he was given 115 gm. commercial glucose, the equivalent of 100 gm. pure dextrose. He slept most of the first period. In the third period the CO_2 and O_2 measurements were lost. The experiment was repeated two days later.

A. P. C., normal control, male, 24 years old, 179.4 cm. tall; medical student in good health.

Jan. 21, 1915, after having been on a low nitrogen diet for several days a basal determination was made.

R. H. S. history in Paper 12.

E. F. B. D. history in Papers 4 and 12.

Emma W., normal control. History in Paper 9. She was in unusually good health and was able to take violent exercise. Her menses were regular and not profuse. On examination of the heart there was a marked respiratory allorrhythmia and also an ocasional premature systole. Several electrocardiographic plates were taken but no abnormal beats photographed, although it was possible to see the typical large diphasic swing of the shadow several times. The first experiment was made May 13, which was the second day of the catamenia. To control this factor a second basal determination was made May 17, the third day after the flow had ceased. She was almost motionless both days while in the calorimeter.

AVERAGE BASAL METABOLISM OF MEN

In Paper 4 the results of respiration experiments on 96 men were considered. To this group may be added the nine men of Palmer, Means and Gamble and the four men studied in the Sage calorimeter, Morris S., Albert G., R. H. S., and A. F. C. If we tabulate the results according to the surface area as determined by Meeh's formula there is no need to change the conclusions expressed in Paper 4. The average of the new cases is 33.6 calories per square meter per hour as opposed to the former figure of 34.7. It does not seem necessary to change the base line again. The greatest variation from the mean is 12.3 per cent. as mentioned previously.

In Paper 4 of this series the results in five cases are given in terms of calories per square meter as determined by the new "Linear Formula." Adding the four new cases of this paper we have a total of nine normal men whose surface area has been accurately measured. The average basal metabolism is 39.7 calories per square meter per hour ("Linear Formula"). The extremes of variation from the average are + 4 per cent. and — 6 per cent. John L., who was 44 years old, could not be found and measured. His results would probably have been further from the average. Means,[5] who measured his nine subjects by the same method, obtained an average figure of 39.6. Until we have a larger number of subjects measured in this manner the figure 39.7, given above, will be considered the standard with which all results are to be compared.

The results obtained by Benedict, Emmes, Roth and Smith may also be recalculated by means of the new "Height-Weight" chart. If we take the seventy-nine men between the ages of 20 and 50, who were of average body shape, and calculate the calories per square meter per

TABLE 1.—Data of—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Albert G.	Prelim.	11:15	.....	.....	.....	.....	.....	.....	.....
12/30/14	1	12:15	23.94	21.20	0.821	30.81	0.418	70.78	74.34
64.91 Kg.	2	1:15	22.70	20.31	0.813	29.14	0.418	67.63	73.41
1.657 Sq. M.	3	2:15	25.40	21.21	0.871	30.47	0.380	71.81	73.78
	4	3:15	24.37	22.30	0.795	30.84	0.380	74.07	74.99
								284.19	
Albert G.	Prelim.	11:12	.....	.....	.....	.....	.....	.....	.....
1/4/15	1	12:13	29.97	23.79	0.916	31.69	0.445	81.53	81.87
65.64 Kg.	2	1:12	29.29	20.73	1.03	29.44	0.445	72.45	77.98
1.665 Sq. M.								153.98	
Albert G.	Prelim.	11:11	.....	.....	.....	.....	.....	.....	.....
1/6/15	1	12:11	32.55	22.59	1.05	30.38	0.509	79.19	77.67
66.16 Kg.	2	1:11	30.64	22.69	0.982	35.28	0.509	78.72	85.06
1.671 Sq. M.	3	2:11	29.03	21.73	0.972	33.60	0.509	75.20	77.68
	4	3:11	24.90	22.03	0.822	34.77	0.509	73.54	81.22
								306.65	
A. F. C.	Prelim.	8:48	.....	.....	.. .	.....	.....	.....	.....
1/21/15	1	9:48	24.17	21.28	0.826	27.28	0.261	71.51	73.07
69.22 Kg.	2	10.48	23.19	20.33	0.830	27.49	0.261	68.44	72.90
1.792 Sq. M.								139.95	
Emma W.	Prelim.	10.41	.....	....	.....	.....	.....	.....	.....
5/13/15	1	11:41	18.22	16.44	0.806	31.75	0.402	54.60	59.93
57.38 Kg.	2	12:41	18.41	16.18	0.827	29.11	0.402	53.94	56.21
1.64 Sq. M.								108.54	
Emma W.	Prelim.	11:00	.....	.....	.....	.....	.....	.....	.....
5/17/15	1	12:00	18.55	16.06	0.840	29.15	0.214	54.18	50.86
57.26 Kg.	2	1:00	18.86	16.77	0.818	27.93	0.214	56.21	52.26
1.64 Sq. M.								110.39	

hour, we obtain the figure 38.9. While this figure is slightly lower than ours, it must be remembered that it was obtained by means of the Benedict apparatus with periods only fifteen to twenty minutes long. For these periods the subjects can remain absolutely motionless, something impossible in calorimeter experiments two to four hours long. It seems preferable to use the average normal obtained in the calorimeter as a standard for pathological cases studied in the same apparatus.

—Calorimeter Experiments

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
.....	37.00	..	..	....	..	..	..	.....	.....	Olive oil, 79 gm. 10:15 a. m.
69.29	36.91	57	12	0.82	16	52	32	1.090	35.59	Asleep 10 min.
79.53	37.03	61	7	0.81	16	54	30	1.042	34.00	Asleep 10 min.
61.51	36.83	64	10	0.88	14	35	51	1.106	36.10	Awake
74.68	36.84	62	13	0.79	13	62	25	1.141	37.24	Awake
285.01										
.. ...	36.88	..	..	....	..	..	..	.....	.....	Commer. glucose, 115 gm.; water, 200 c.c., 10:13 a.m.
94.63	37.12	65	7	0.94	15	17	68	1.242	40.73	Asleep
72.76	37.03	59	17	1.08	16	0	84	1.104	36.35	Awake
167.39										
.....	36.94	..	..	....	..	..	..	.....	.....	Com.glu., 115 gm.; lemon juice, 1 c.c.; water, 125 c.c. at 10:11 a. m.
74.37	36.89	66	11	1.11	17	0	83	1.197	39.32	Quiet
84.19	36.88	64	29	1.02	17	0	83	1.190	39.09	Quiet
75.70	36.85	..	30	1.01	18	0	82	1.137	37.34	Restless
72.69	36.70	57	15	0.83	18	47	35	1.112	36.51	Fairly quiet
307.15										
.....	36.89	..	..	....	..	.	..	.....	.....	Basal; low nitrogen diet
61.25	36.69	68	30	0.83	10	52	38	1.033	34.45	Restless
60.55	36.48	74	20	0.84	10	70	20	0.989	32.97	Restless
121.80										
.....	37.04	..	..	....	..	..	..	.....	.....	Basal; 2d day of catamenia
54.68	36.93	60	2	0.81	20	52	28	0.952	29.80	Almost motionless
49.75	36.80	58	6	0.83	20	46	34	0.940	29.44	Almost motionless
104.11										
.....	36.91	..	..	....	..	..	..	.....	.....	Basal
46.26	36.82	57	4	0.85	10	46	44	0.946	29.61	Almost motionless
55.75	36.90	55	4	0.82	10	55	35	0.982	30.72	Almost motionless
102.01										

If we apply the "Height-Weight Formula" to the averages of the 68 women given by Benedict and Emmes[7] on page 256, we find that the approximate surface area for the average weight of 54.5 kg. and average height of 162 cm. is 1.57 sq. meters. This would make their average heat production per hour 35.9 calories per sq. meter, and if

7. Benedict and Emmes: A Comparison of the Metabolism of Normal Men and Women. Jour. Biol. Chem. 1915, xx, 253.

TABLE 2.—Summary of Results with Normal Subjects
(all men except emma w.)

Name	Age, Years	Average Weight, Kg.	Height, Cm.	Sq. M. Surface Area		According to Meeh's Formula		According to Linear Formula	
				Meeh's Formula	Linear Formula or Measured	Cal. per Sq. M. per Hour	Variation from Average, per Cent.	Cal. per Sq. M. per Hour	Variation from Average, per Cent.
Morris S.	22	61.21	164.3	1.912	1.644	35.2	+1	41.2	+ 4
Albert G.	24	65.90	162.2	2.009	1.667	34.3	—1	41.2	+ 4
R. H. S.*	21½	64.36	184.2	1.977	1.830	34.6	—0	37.4	— 6
E. F. D. B.	33	74.64	179.2	2.183	1.906	32.9	—6	37.7	— 5
A. F. C.	24	69 22	179.4	2.076	1.792	33.7	—3	39.1	— 2
Emma W.*	26	57.32	164.8	1.831	1.642	29.9	—8	33.3	—10
Average for men						34.7	...	39.7	
Average for women						32.3	...	37.0	

* Unusually quiet subjects

TABLE 3.—The Basal Metabolism Determination of Average Normal for Men Between Ages of 20 and 50 *

Name	Details Published in Paper	Average Calories per Sq. M. per Hour, Linear Formula
G. L.	4	40.7
E. F. D. B.	4 and 11	39.4†
R. H. H.	4	40.9
L. C. M.	4	40.5
F. C. G.	4	37.7
Morris S.	7	41.2
Albert G.	11 and 13	41.2
R. H. S.	11	37.4
A. F. C.	13	39.1
Average, Sage normal controls		39.7
Average, Means' normal controls		39.6
Average, Benedict s normal controls		38.9

* Average calories per square meter per hour, acording to the "Linear Formula," of men examined in Sage calorimeter. It has been impossible to find John L. and measure his surface area.

† Average of four basal experiments, Paper 4, first experiment Paper 11.

we add to the group the seven women studied by Means[5] the average for the whole would be 36.9 calories, a figure which may be adopted as the standard for normal women. This shows that the metabolism of women is about 7 per cent. lower than that of men, a figure in agreement with the conclusions of Benedict and Emmes.

TABLE 4.—A Comparison of the Metabolism of Fat and Thin Subjects Taken Largely from the Work of Benedict, Emmes, Roth and Smith

Name	Per Cent. Deviation from Normal Average, 34.7 / 29.7		Calories per Kg. per 24 Hours	Name	Per Cent. Deviation from Normal Average, 32.3 / 36.9		Calories per Kg. per 24 Hours
	Meeh's Formula	Height-Weight Formula			Meeh's Formula	Height-Weight Formula	
Fat Men—				Fat Women—			
W. S.	— 1.2	+ 5.0	22.8	Dr. M. D.	—11.2	— 1.0	18.9
O. F. M.	— 8.6	— 0.5	21.3	O. A.	— 9.6	0.0	19.5
Prof. C.	—15.1	—12.0	19.9	H. H.	—17.0	— 7.0	18.0
F. E. M.	— 6.9	— 4.0	22.7	H. D.	—10.3	+ 1.0	20.1
F. A. R.	— 6.1	— 3.0	22.9	F. M. R.*	— 6.8	+ 7.0	21.0
				D. L.*	—13.5	+ 1.0	19.7
				L. F. W.*	—16.9	0.0	18.6
Average	— 7.6	— 4.0	21.9	Average	—12.2	0.0	19.4
Thin Men—				Thin Women—			
R. A. C.	+11.3	— 2.0	29.7	J. T.	+12.5	+ 2.0	31.7
B. N. C.	+ 7.2	— 6.0	29.8	A. A.	+ 9.6	— 5.0	32.0
L. E. A.	+ 7.6	— 2.0	29.5	E. W.	—12.2	+ 7.0	31.5
A. F. G.	— 0.8	—10.0	27.0	A. C.	— 0.5	— 8.0	27.4
				J.	— 2.1	— 7.0	26.9
				L. B.	— 6.7	—13.0	24.9
Average	+ 6.4	— 5.0	29.0	Average	+ 4.2	— 4.0	29.1

* Means' subjects.

A COMPARISON OF FAT AND THIN SUBJECTS

In Paper 4 of this series attention was called to the fact that in the case of fat individuals Meeh's formula would give a figure for the calories per square meter which would be very much too low. It might have been added that in the case of thin subjects the figure would be very much too high. The male subjects of Benedict and co-workers were plotted in our previous paper according to height and weight, and on account of the above mentioned errors six fat men and two thin ones were excluded from the averages. Now that it is possible to correct the error in Meeh's formula it has seemed advisable to compare

the metabolism of the fat and thin groups. A table compiled by the insurance companies showing the average weight of the male applicants between the ages of 25 and 29 years for different heights was taken as a standard. Those subjects whose weight departed more than 20 per cent. from this standard were considered either fat or thin. H. F. was excluded on account of old age, two more thin men, L. E. A. and A. F. G., were included in the new list. The fat and thin women were tabulated and three stout subjects of Means[5] added to the list. The results given in Table 4 are expressed in terms of variation from the averages for all normal controls, 39.7 calories per sq. meter per hour "Linear Formula" for the men and 36.9 for the women. According to body weight the fat and thin groups show a difference of 41 per cent.; according to Meeh's formula 15 per cent., according to the "Linear Formula" 3 per cent. This shows that Rubner's law that metabolism is proportional to surface area holds for fat and thin subjects and that we can safely use our new baseline for hospital patients whether they be fat or thin.

TABLE 5.—Basal Metabolism of Normal Men and Women 40 to 60 Years Old, Recalculated in Terms of Surface Area by the "Height-Weight" Formula

Subject	Investigators	Age, Years	Per Cent. Deviation from Average Cal. per Sq. M. per Hr. (20-50 Yrs.)
Men			Av. 39.7
A. L.	B. E. R. and S.	40	— 2.0
F. G. B.	B. E. R. and S.	41	— 8.0
Dr. P. R.	B. E. R. and S.	41	—12.0
Dr. S.	B. E. R. and S.	43	—20.0
Prof. Z.	M-L. and F.	43	— 5.0
John L.	G. and D. B.	44	—12.0
G. L.	G. and D. B.	47	+ 3.0
W.	M-L. and F.	56	— 5.0
E. J. W.	B. E. R. and S.	58	—17.0
Women			Av. 36.9
B. K.	M-L. and F.	40	+10.0
Mrs. H. D.	B. E. R. and S.	42	+ 1.0
Dr. M. D.	B. E. R. and S.	44	— 1.0
Mrs. S. C.	B. E. R. and S.	52	—12.0
Mrs. E. B.	B. E. R. and S.	53	— 1.0
Average, men and women		40 to 50	— 4.3
Average, men and women		50 to 60	—11.3

INFLUENCE OF AGE

In Table 5 are grouped the corrected results for the normal controls between 40 and 60 years of age. In Paper 4 the subjects between the ages of 20 and 50 were grouped together, but it is apparent that the average metabolism between the ages of 40 and 50 is 4.3 per cent. lower than that of the whole group, while those between 50 and 60 are 11.3 per cent. lower. It is necessary to use a lower figure for the baseline after the age of 50, and perhaps advisable to make the change at the age of 40.

VARIATIONS IN METABOLISM

We have already spoken of the extremes in the oxygen consumption of the same individual during the course of months and years as reported by Benedict. Only a few of the subjects here reported have been studied over long enough periods to give much evidence on the question. The basal metabolism of E. F. D. B. was 35.91 calories per square meter per hour on March 13, 1913, the first time he was in the calorimeter, when he was somewhat restless. In May, 1913, it was 33.29; in March, 1914, 34.09; May, 1914, 32.97; May, 1915, 32.86. The extreme range was 9 per cent., and, excluding the first experiment, 3.7 per cent. Albert G. showed a variation of 6.4 per cent., the metabolism being unusually low on December 28, when he dozed during the two-hour experiment. In Paper 7 it will be noted that the curves representing the metabolism of the typhoid patients are very uniform.

INFLUENCE OF FOOD

In a footnote to Paper 4 it was stated that Morris S. showed a rise of 6.5 per cent. in metabolism two to six hours after a meal containing 9.6 gm. nitrogen. On recalculation the rise during the period turns out to be 7.4 per cent., and if we exclude the third period when he slept forty minutes, 11.9 per cent. This corresponds with the rise of 12 per cent. found in the case of E. F. D. B. after a similar meal containing 10.5 gm. nitrogen. Albert G. on January 6, one to four hours after 115 gm. of commercial glucose, the equivalent of 100 gm. dextrose, showed an average metabolism 11 per cent. higher than the basal determination two days later. This corresponds with the average of 9 per cent. obtained with G. L. and E. F. D. B. in the previous investigation. The one experiment on Albert G. one to five hours after 79 gm. olive oil showed little increase in metabolism. Fat exerts its chief specific dynamic action in the period immediately succeeding the hours studied. The glucose experiment on Albert G. January 4 was too short to be of value.

TABLE 6.—Water Elimination Through Skin and Lungs. Normal Controls in Calorimeter. Basal Metabolism Experiments

Name and Date	Average H_2O Gm. per Hr.	Average Calories per Hr. Dir. Cal.	Per Cent. Cal. Lost through Vaporization	Per Cent. Deviation from Mean 23.9%
G. L. 3/11/13	37.44*	80.88	27.3*	+14
E. F. D. B. 3/13/13	27.22	75.20	21.1	—12
5/17/13	32.30	71.44	26.4	+10
3/30/14	30.52	75.78	23.5	— 2
5/18/14	28.06	68.69	23.9	± 0
5/ 6/15	32.21	72.71	25.9	+ 8
F. C. G. 3/17/13	19.45	57.19	19.9	—17
4/22/13	27.44	60.72	26.4	+10
R. H. H. 3/19/13	28.41	69.77	23.8	— 0
Louis M. 3/26/13	27.15	67.40	23.6	— 1
John L. 3/26/14	24.78	61.10	23.7	— 1
L. C M. 5/ 4/14	27.80	70.21	23.1	— 3
Albert G. 12/21/14	31.58	71.68	25.7	+ 7
12/28/14	26.12	71.20	21.4	—10
1/ 8/15	29.37	69.82	24.6	+ 3
R. H. S. 4/19/15	26.27	72.03	21.3	—11
Morris S. 12/17/14	27.06	70.33	22.5	— 6
A. F. C. 1/21/15	27.39	60.90	26.3	+10
Av 18 experiments on men.....	28.4	.....	23.9	....
Emma W. 5/13/15	30.43	52.06	34.1	+42
5/17/15	28.54	51.01	32.6	+36

* Much more warmly dressed than the other subjects.

WATER ELIMINATION

In Table 6 the water elimination from skin and lungs is given for the twenty basal experiments on normal adults. The first column expresses the averages for each experiment in grams per hour. Each gram vaporized at 23 C. represents the loss of 0.584 calories. The second column gives the average calories produced per hour as measured by the method

of direct calorimetry. The third represents the percentage of calories lost through vaporization. It will be seen that normal men dressed in underwear and pajamas in a well ventilated box at 23 C. give off between 19 and 32 gm. of water per hour, dissipating in this manner between 20 and 27 per cent. of the total heat produced. The average figures are 28.4 gm. per hour and 23.9 per cent. of the calories. Eighty-three per cent. of the eighteen experiments come within 10 per cent. of this last figure.

There are many factors which influence the amounts of water given off by skin and lungs, the most important being the amount of water previously ingested, the amount of clothing, the temperature and humidity of the air and the rise or fall of body temperature. The amounts eliminated in consecutive hours may vary greatly and even transient emotions may cause sweating. The subject is too complicated to be treated in this short paper and is reserved for later discussion.

TABLE 7.—Standards of Normal Metabolism. Average Calories Per Hour Per Square Meter of Body Surface

Subjects, Age in Years	According to Meeh's Formula	According to Linear and Height-Weight Formulas
Boys, 12 to 13	45.7	49.9
Men, 20 to 50	34.7	39.7
Women, 20 to 50	32.3	36.9
Men, 50 to 60	30.8	35.2
Women, 50 to 60	28.7	32.7

SUMMARY AND CONCLUSION

The basal metabolism of four normal men and one woman has been determined and experiments have been made on the specific dynamic action of protein and glucose. A study of the new controls, together with those reported in the literature since our last publication, supports the views previously expressed. There is no reason to change the statement made in our previous paper, that if a given subject's basal metabolism is more than 10 per cent. from the average, it may be regarded as abnormal, but cannot be proved abnormal unless the departure from the average is at least 15 per cent. The average basal metabolism of normal men is 34.7 calories per square meter per hour as determined by Meeh's formula. On account of the average plus error of about 15 per cent. in Meeh's formula the average figure is 39.7 calories, or in round numbers 40 calories, when the more exact "Linear Formula" or the new "Height-Weight Formula" is used to determine surface area.

The average metabolism of fat and thin subjects is the same according to surface area when the surface area is correctly measured. The metabolism of women averages 37.0 calories, or 6.8 per cent. lower than that of men. A group of men and women between the ages of 40 and 50 gave figures 4.3 per cent. below, and a group 50 to 60 years old 11.3 per cent. below the average for the larger group between the ages of 20 and 50.

Under the atmospheric conditions of the calorimeter experiments the average water elimination by normal men through skin and lungs is 28.4 gm. an hour. About 24 per cent. of the heat produced is dissipated in the vaporization of water.

The figures for the specific dynamic action of protein and glucose previously obtained are confirmed. A table of normal standards is given.

CLINICAL CALORIMETRY

FOURTEENTH PAPER

METABOLISM IN EXOPHTHALMIC GOITER*

EUGENE F. Du BOIS, M.D.
NEW YORK

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To those who are accustomed to think in terms of the energy requirement, exophthalmic goiter stands out *par excellence* as the disease of increased metabolism, and the increased metabolism stands out as the chief symptom of hyperthyroidism. The determination of the heat production seems to afford the best index of the severity and course of the disease. There is great need of some purely objective test in hyperthyroidism to indicate the effect of treatment, since psychotherapy can modify profoundly all subjective symptoms. At present the scientific status of the treatment of exophthalmic goiter is about at the point where we would be with diabetes if there were no laboratory tests for glucose and the acetone bodies.

No one of the simpler objective tests taken alone gives an accurate idea of the course of the disease; but when a number are taken together and added to the clinical impression of the observer, they afford a rough measure of the severity of the case. The rapidity of the heart action is perhaps the best guide, but the heart is often affected by other conditions, and damage to the heart may outlast the other symptoms. Rise in temperature is so irregular as to preclude its use as a reliable

* Submitted for publication Feb. 4, 1916.

* From the Russell Sage Institute of Pathology, in Affiliation with the Second Medical Division of Bellevue Hospital.

index. Changes in the size of the gland do not parallel the course of the disease. Changes in weight, warmth of skin and sweating are but consequences of the increase in heat production. Eye symptoms, tremor, nervous irritability, weakness, diarrhea are all too variable to be of reliance and are too difficult to measure accurately. The blood pressure is of some use as a guide, but it is affected by age and the condition of the cardiovascular system. The sugar tolerance depends on other ductless glands as well as the thyroid, and even in health has wide limits. The mononucleosis which has been considered characteristic by Kocher, Halsted and others is found in other diseases, and does not seem significant enough to be our main reliance.

In contrast to the above mentioned symptoms, an increased basal metabolism is found with great regularity in exophthalmic goiter, and in severe cases reaches a level found in no other condition. On the other hand, in cretinism and myxedema the metabolism is lower than in any other disease. The administration of thyroid extract, particularly in myxedema, raises the heat production. All other diseases in which metabolism is increased are easily distinguishable from exophthalmic goiter, and they never approach the extremes found in this condition. The basal metabolism is higher than normal in youth, in fever, in lymphatic leukemia and pernicious anemia, in severe cardiac disease, and in some cases of severe diabetes and cancer. It is lower than normal in old age, in some wasting diseases and perhaps in some cases of obesity. Diseases of the ductless glands other than thyroid show in some cases an increase, in some a decrease; but these are comparatively small.

The theories of exophthalmic goiter at present are in a somewhat chaotic state. The suprarenals, thymus and most of the other ductless glands are thought by many to be involved, and the symptoms have lately been divided into sympatheticotonic and vagotonic groups. Even in regard to the thyroid itself some advance the theory of dysthyroidism in addition to or in place of hyperthyroidism. Such confusion is natural when we have few objective tests and many bizarre symptoms which can be ascribed at will to various ductless glands whose functions are obscure. It would seem as if we needed more laboratory work for those who hold no brief for any particular kind of therapy. Even the most extreme advocates of the new theories ascribe the chief rôle to an overactivity of the thyroid gland. For the purpose of simplicity in this paper one may consider the symptoms of exophthalmic goiter to be caused by too much thyroid secretion, and allow the reader to select for himself those cases in which he believes other glands to be involved.

PREVIOUS STUDIES OF THE RESPIRATORY EXCHANGES

The question of the metabolism in exophthalmic goiter has been reviewed by Magnus-Levy,[1] Hirsch,[2], and Falta;[3] Scholz[4] has given a large number of references on the subject of cretinism.

Friedrich Müller,[5] in 1893, first pointed out the increase in metabolism in exophthalmic goiter by showing that a patient lost weight and nitrogenous substances on a diet that was more than sufficient to cover the needs of a normal person. Magnus-Levy[6] two years later was the first to demonstrate the increase in the respiratory metabolism in hyperthyroidism and the decrease in myxedema. Since then he has studied many cases of both diseases and has used the respiratory metabolism as an index of the effects of treatment, thus demonstrating the increase in heat production following the administration of thyroid extract. He found that in myxedema the rise in heat production began in the first week of the administration of the extract and increased gradually till the fourth or fifth week. The effect was most pronounced in severe cases, causing a rise of from 50 to 70 per cent. In the mild cases the increase was slight, never going above 20 per cent., and in five of the nine normal controls there was no rise at all. Stüve,[7] who worked with Magnus-Levy, found that thymus extract had no effect on the heat production. Magnus-Levy and Stüve found the metabolism greatly increased in exophthalmic goiter, and their results, together with those of the others who have studied this subject, are recorded in Table 1. Thiele and Nehring,[8] and Anderson and Bergman[9] studied the influence of thyroid extract, the former finding an increase in the metabolism of obesity patients after its use and the latter no increase with two normal men.

1. Magnus-Levy: Von Noorden's Handbuch der Pathologie des Stoffwechsels, Berlin, 1906.

2. Hirsch, Rahel: Oppenheimer's Handbuch der Biochemie, iv, 2, 165.

3. Falta: Die Erkrankungen der Blutdrüsen, Berlin, 1913.

4. Sholz: Klinische und Anatomische. Untersuchungen über den Cretinismus, Berlin, 1906.

5. Müller, Friedrich: Beiträge zur Kenntniss der Basedowische Krankheit, Deutsch. Arch. f. klin. Med., 1893, li, 335.

6. Magnus-Levy: Gaswechsel bei Thyroidea, Berl. klin. Wchnschr., 1895, xxxii, 650; Untersuchungen zur Schilddrüsenfrage, Ztschr. f. klin. Med., 1897, xxxiii, 269; Ueber Myxoedem, ibid, 1904, lii, 201.

7. Stüve: Respiratorische Gaswechsel bei Schilddrüsenfutterung Morbus Basedowii u. s.w., Fest. Stadt. Krankenh., Frankfurt a. M., Mahlau, 1896.

8. Thiele and Nehring: Untersuchungen des respiratorischen Gaswechsel unter dem Einflusse von Thyreoideapraparaten und bei anaemischen Zustanden des menschen, Ztschr. f. klin. Med., xxx, 41.

9. Anderson and Bergmann: Einfluss der Schilddrüsenfutterung auf den Stoffwechsel des gesunden Menschen, Skand. Arch. f. Physiol., 1898, viii, 326.

TABLE 1.—Goiter Cases in the Literature Arranged—

Observer	Patient	Sex*	Age, Years	Duration of Disease, Years	Clinical Classification
Hirschlaff	Louise B.	♀	..	9	Very severe last ten days of life
Author	Case 6 (Anna K.)	♀	26	10	Severe
Author	Case 3 (James McE.)	♂	29	[illegible]	Severe
					100% above average for women
Salomon	R. H.	♂	40	11	Five months before death
Hirschlaff	Louise B.	♀	21	9	Severe first two months in hospital
Magnus-Levy	Frl. E. B.	♀	20	..	Severe; acute
Salomon	Fall I	♂	23	5	
Magnus-Levy	Fr. Kr.	..	26	26	Very severe; pregnant six months
Undeutsch	Ja.	♀	24	½	"Ziemlich Schwer"
Author	Case 1 (Max W.)	♂	40	1⅓	Severe
Magnus-Levy	Hr. G.	♂	25	..	Severe
Undeutsch	K.	♀	23	4	(Mod. severe?)
Magnus-Levy	Frau Schr.	♀	42	..	Very severe
Pribram and Porges	E. Tesch.	♀	23	2	(Mod. severe?)
Author	Case 2 (Edwin T.)	♂	20	½	Acute; mod. severe
Pribram and Porges	M. S.	..	25	½	(Acute; mod. severe ?)
Salomon	M. J.	♀	25	1½	(Mod. severe?)
Magnus-Levy	Frl. E. T.	♀	22	..	Severe
Magnus-Levy and Stüve	Fr. R. B.	♀	26	..	Severe
Author	Case 4 (Dr. G. S. L.)	♂	52	3-4	Severe
Salomon	Fall II	♀	19	½	
					30% above average for women
Magnus-Levy	Hr. J.	♂	20	..	Severe
Falta	J. H.	..	22	..	(Mild?)
Falta	R. Fl.	♀	3½	3	(Severe?)
Author	Case 9 (Marion B.)	♀	22	3	Mild; operated
Author	Case 8 (Sarah M.)	♀	29	8	Mild; operated
Magnus-Levy	Frl. Ung.	♀	55	..	Severe
Author	Case 7 (Anna R.)	♀	29	5	Moderately severe
Author	Case 10 (Margaret L.)	♀	51	1	Atypical cardiac
Magnus-Levy	M. P.	♂	11½	..	Small struma, otherwise normal
Magnus-Levy	Fr. O.	♀	54	..	Simple goiter
Stüve and Magnus-Levy	Frl. G. W.	♀	24	..	Severe

—According to the Level of the Respiratory Metabolism

Calories per Sq. M. per Hr. Meeh	Pulse Rate	Blood Pressure, Syst.	Enlargement of Heart to Left, Cm.	Enlargement of Thyroid	Exophthalmos	Von Graefe Sign	Mental Irritability	Tremor	Warmth of Skin	Emaciation	Remarks
72.1											
66.1	122	.....	0	+	+	±	++	+	++	+	After ligation of 2 arteries
65.0	100-124	130-146	3.5	++	+	+	++	+	++	++	Alcoholic
64.6											
61.7	110-120	.....	0	+	—	—	+	....	.....	++	
61.7	100-130	.....	±	+	++	++	++	+	++	+	
60.0	120										
58.0	++	.....	+	+	++	++	+	+	+	++	
57.2	142										
56.6	++	.....	+	+	+	—	++	++	+	+	
55.4	100-136	130-150	2.5	++	++	±	+++	+	++	±	
54.4	112										
53.7	92-122	.....	+	+	++	....	....	+			
53.1	130-150										
53.0	++	.....	+	..	....	....	+	+			
50.6	92-112	140-150	0	+	+	±	++	+	++	±	
50.2	++	.....	+	+	+	+	....	+			
49.7	90-100	.....	±	+	—	—	+	+	+	±	
49.6	100										
49.3											
49.2	97-101	148	2	++	+	+	+	++	++	+	After ligation of 4 arteries
48.7	90-124	.....	+	+	+	+	....	....	.....	±	
48.5											
46.1	122										
44.8	.....	.....	..	..	—	—	....	+	+		
44.5	80-150	130	..	+	+	++	++	+	++		
44.1	.....	.....	..	..	+	....	+	....	+	·	Par. thyroidect. 2 and 1 yrs. ago
43.8	.....	.....	0	+		-	+	+	±	....	Partial thyroidectomy 8 yrs. ago
43.5	120										
43.4	84-92	.....	0	+	+	+	+	+	+	+	
42.0	68-88	170	2-3	++	+	+	+	....	++	+	
40.6	Fibril	.....	—	±	—	—	....	—	.....	—	
40.6	94										
39.9	100-120										

TABLE 1.—

Observer	Patient	Sex*	Age, Years	Duration of Disease, Years	Clinical Classification
Magnus-Levy	Frl. M. Kr.	♀	20	..	Mild
Falta	Ad. K.	♂	33	..	Severe
Undeutsch	Wit.	♀	24	14?	"Forme fruste"
Magnus-Levy	Hr. Be.	♂	20	..	Mild
Magnus-Levy	Frl. E. W.	♀	21	.	Severe
Magnus-Levy	Fr. B.	♀	52	..	Half way between Kropf and forme fruste
Author	Case 5 (Peter N.)	♂	23	5	Atypical; operated
					Upper normal limit for women
Magnus-Levy	Hr. R. B.	♂	20	..	Mild
					Average for normal men
Magnus-Levy	Frl. U.	♀	55	..	Typical; mild
Author	Case 11 (Miss B. H.)	♀	31	4	Atypical; operated
Magnus-Levy	Frl. E. D.	♀	25	..	Simple goiter
Magnus-Levy	Frl. Sch. M.	♀	28	..	Mild
Magnus-Levy	Frl. M. Kl.	♀	17	..	Simple goiter
					Average for normal women
Magnus-Levy	Frl. Rh.	♀	36	..	Half way between Kropf and forme fruste; simple goiter

* In this column, ♂ denotes male and ♀ female.

Hirschlaff[10] made one of the most valuable contributions to the subject by studying in great detail over a long period a very severe case of hyperthyroidism which eventually came to necropsy. The oxygen consumption of this patient was about 77 per cent. above normal, rising to 105 per cent. above normal in the last week of life. Magnus-Levy considers that some of the high results on this patient were due to restlessness, but some were obtained while she was under the influence of morphin. This careful laboratory work on one patient is of more value to science than the clinical observation of a hundred patients. Jaquet and Svenson[11] found no constant rise in metabolism when they treated cases of obesity with thyroid extract. They also studied the specific dynamic action of food on these patients, and concluded that it was less than normal before treatment with thyroid

10. Hirschlaff, W.: Zur Pathologie und Klinik der Morbus Basedowii, Ztschr. f. klin. Med., 1899, xxxvi, 200.

11. Jaquet and Svenson: Zur Kentniss des Stoffwechsel fettsuchtigen Individuen, Ztschr. f. klin. Med., 1900, xli, 375.

—(*Continued*)

Calories per Sq. M. per Hr. Meeh	Pulse Rate	Blood Pressure, Syst.	Enlargement of Heart to Left, Cm.	Enlargement of Thyroid	Exophthalmos	Von Graefe Sign	Mental Irritability	Tremor	Warmth of Skin	Emaciation	Remarks
39.7	80										
39.7	120-140	140	2	++	-	—	+	++.	++	+	
37.7	100+	125	0	+	—	—	++	++	+	±	
37.0	78										
36.5	128										
35.7	96	.....	±	+	-	—	....	±			
35.5	72-94	.....	1	±	—	—	+	++	—	+	Four arteries ligated 1 yr. ago
35.5											
34.7											
34.7											
34.7	88-90										
34.6	72-96	112-120	0	—	±	—	++	+	—	+	Par. thyroidect. 2 mos. ago
34.6	86										
34.1	80										
3.30											
32.3											
29.4	72-92	.....	0	±	±	+	....	±	.....	....	Hysterical temperament

extract but greater than normal after treatment. Salomon[12] considered the increase in metabolism to be the most important objective symptom of hyperthyroidism, and followed it during treatment with "Radogen" and the serum of a thyroidectomized horse. Neither of the remedies caused a fall in the metabolism. Steyrer[13] studied the effects of thyroid tablets on one exophthalmic goiter and one myxedema patient, using a Pettenkofer-Voit respiration chamber. Pribram and Porges,[14] working under Salomon, studied the "nüchtern" or basal metabolism from fifteen to seventeen hours after the last meal of diets containing various amounts of nitrogen. They found the heat production from 4 to 8 per cent higher the morning after a diet containing from 31 to 42

12. Salomon, H.: Gaswechseluntersuchungen bei Morbus Basedowii und Akromegalie, Berl. klin. Wchnschr., 1904, xxiv, 635.

13. Steyrer, A.: Ueber die Stoff und Energieumsatz bei Fieber, Myxoedem und Morbus Basedowii, Ztschr. f. exper. Path. u. Therap., 1907, iv, 720.

14. Pribram and Porges: Ueber den Einfluss verschiedenartiger Diätformen auf den Grundumsatz bei Morbus Basedowii, Wien. klin. Wchnschr., 1908, xxi, 1584.

gm. of nitrogen than after mixed diets rich in carbohydrate. They do not consider that this differs from what would be found in normal persons after such excessive protein feeding, and believe that the basal metabolism is not much influenced by protein or meal abstinence. In one patient two treatments with the Roentgen ray did not cause any drop in the oxidative processes. More recently Undeutsch,[15] using the Rolly-Rosiewicz modification of the Benedict universal respiration apparatus, compared the rise in metabolism following the administration of various forms of protein to patients with exophthalmic goiter. He found that 40 gm. of Aleuronat increased the metabolism more than 35 gm. Roborat, and that both had greater action than 200 gm. chopped beef. Two normal controls gave the same results. He concludes that animal protein has a lower specific dynamic action than vegetable. Undeutsch also made observations on three of his patients from one to two weeks after a partial thyroidectomy. One patient showed a drop of more than 10 per cent. in the heat production, one a drop of 20 per cent. and a third with "forme fruste" and colloid goiter only a slight reduction.

Von Bergman[16] studied several myxedema patients, finding the metabolism moderately decreased. He observed a rise of 25 per cent. in the heat production in an obesity patient after the administration of thyroid extract. Falta[3] reports respiration experiments on three of his exophthalmic goiter patients made by Dr. Bernstein. Means,[17] studying several obesity patients and making a large number of respiration experiments on one marked case, found a marked rise in metabolism after thyroid administration.

The literature on the treatment of exophthalmic goiter is too enormous to be reviewed in this paper, and only those remedial measures used on the patients here described will be discussed. A partial thyroidectomy has been and perhaps always will be the standard method of treatment. Recently many surgeons have been ligating one or more of the thyroid arteries under local anesthesia as a preliminary to the more radical operation or in place of it. Medical treatment gives slower results which are often very satisfactory. Mental and physical rest over long periods of time, combined with abundant food, almost invariably improves the patient's condition, and in many cases there is a tendency toward recovery without any treatment. Beebe and

15. Undeutsch, W.: Experimentelle Gaswechseluntersuchungen bei Morbus Basedowii; Grundumsatz und Umsatz nach Aufnahme von animalischem und vegetabilischem Eiweiss, Inaug. Dessert., Leipzig, 1913.

16. Von Bergman: Der Stoff und Energieumsatz beim infantilem Myxoedem und beim Adipositas universalis mit einem Beitrage zur Schilddrüsenwirkung, Ztschr. f. exper. Path. u. Therap., 1909, v, 646.

17. Means: Studies of the Basal Metabolism in Obesity and Pituitary Disease, Jour. Med. Research, 1915, xxxii (New Series, xxvii), 121.

Rogers,[18] and more recently Beebe[19] alone, have used a cytotoxic serum prepared by injecting sheep with an extract of human thyroid tissue. This serum has never come into general use. Some patients cannot take the serum on account of violent local and constitutional reactions, and others who can take it show little improvement, as is the case with all other forms of treatment. Rogers[20] uses partial thyroidectomy in some cases, and serum in a few others, but places his chief reliance on ligation of two or more of the thyroid arteries as giving the best results in the long run. He has used thyroid extract in some cases for a few days after the ligation, and in other asthenic patients has given a thyroid preparation called "X Thyroidin," or thyroid "residue." Forcheimer[21] is very enthusiastic about the quinin-ergotin treatment which he devised several years ago. He gives quinin hydrobromate, 5 grains, and ergotin, 1 grain in gelatin coated pills four times a day. All of the foregoing clinicians insist on rest from work and mental relaxation as part of the treatment.

Plummer[22] has recently abstracted the histories of the unusually large number of cases treated at the Mayo Clinic, and on the basis of averages has arranged the symptoms in the order of their onset as follows: (1) cerebral stimulation; (2) vasomotor disturbances of the skin; (3) tremor; (4) mental irritability; (5) tachycardia; (6) loss of strength; (7) cardiac insufficiency; (8) exophthalmos; (9) diarrhea; (10) vomiting; (11) mental depression; (12) jaundice; (13) death. Of especial interest is the work of Rudinger[23] on the nitrogen minimum in hyperthyroidism. He places his patients on Landergren's low nitrogen diet, and found the nitrogen output to be so much greater than in normal persons that he considers there is a 100 per cent. increase in the destruction of body nitrogen on the fourth day of the diet. In regard to the discussion as to whether we are dealing with a hypersecretion or abnormal secretion of the thyroid, it may be well to call attention to the statement of Magnus-Levy, "The quantitative relations

18. Rogers, John, and Beebe, S. P.: The Treatment of Hyperthyroidism by a Specific Cytotoxic Serum, The Archives Int. Med., 1908, ii, 297.

19. Beebe, S. P.: The Serum Treatment of Hyperthyroidism, Jour. Am. Med. Assn., 1915, lxiv, 413.

20. Rogers, John: The Course of Acquired Disease of the Thyroid Gland and the Principles which Seem to Control Its Progress, Ann. Surg., 1914, p. 281; Exophthalmic Goiter and Its Treatment, New York State Jour. Med., 1915, xv. 4; Am. Jour. Physiol, 1915, xxxvi, 113; ibid., 1915, xxxvii, 121, 453; ibrid., 1915, xxxix, 154; ibid., 1916, xxxix, 345.

21. Forcheimer, F.: Exophthalmic Goiter, in Therapeusis of Internal Diseases, 1913, iii, 895.

22. Plummer, H. S.: The Clinical and Pathologic Relationships of Hyperplastic and Nonhyperplastic Goiter, Jour. Am. Med. Assn., 1913, lxi, 650.

23. Rudinger: Ueber den Eiweissumsatz bei Morbus Basedowii, Wien. klin. Wchnschr., 1908, xxi, 1581.

of thyroid secretion are almost totally unknown, and are much too complicated to allow our following out a theory of hyperthyreosis in all its details; much less . . . does it enable us to argue a theory of dysthyreosis." Falta, Newburgh and Nobel,[24] on the basis of experiments with various organ extracts, believe in "Ueberfunction" rather than "Dysfunction" in exophthalmic goiter, and consider that the difference in symptoms is due to differences in the constitution of the patient.

METHODS OF EXPERIMENT

Most of the patients studied over considerable periods of time remained in the metabolism ward described in Paper 3 of this series. They were placed in the respiration calorimeter in the morning hours, either without breakfast or after special meals, if the tests were being made to determine the specific dynamic action of food. Each patient was put in the calorimeter for half an hour or so a day or two before the first experiment, in order to let him become accustomed to the interior of the apparatus. No patient objected, since all realized that their treatment was being controlled by the results of the observations. Some of the patients had marked tremors when they moved, but inside the calorimeter they were lying quietly on a comfortable bed, and they moved but seldom. The work-adder was of great service in giving an accurate idea of the relative activity of the subject in each period. In the severe cases with moist skin, the work-adder was even more sensitive than usual, since any movement on the part of the patient liberated an abnormal amount of moisture from the bedding and clothing, expanding the air of the box to a marked degree. This accounts for some of the high readings of this instrument; but some of the patients with severe cases were distinctly restless, particularly toward the end of an observation. It was for this reason that short experiments were used by preference.

The female patients were taken directly from the general medical or surgical wards. A few of both sexes came to the calorimeter room from their homes in the neighborhood, lying down for at least two hours before the observation began. Great care was taken to avoid fatigue or excitement, since it was apparent that the metabolism of these thyroid patients showed great lability.

CASE HISTORIES

CASE 1.—*History.*—Max W., aged 40, storekeeper, born in Roumania, Hebrew, admitted Feb. 11, 1914. Had typhoid fever when 18 years old. Two years ago he was operated on for inguinal hernia. About this time he was refused life insurance because he weighed 190 pounds. He drinks little, but smokes from fifteen to twenty cigarets a day.

24. Falta, Newburgh and Nobel: Ztschr. f. klin. Med., 1911, p. 72.

Present Illness.—In January, 1913, he received news of the violent death of his brother, and was much excited for a week. The next month he suffered from a severe unproductive cough, was nervous and lost weight. He was sent to the mountains with a diagnosis of tuberculosis, but did not improve. The Wassermann reaction was found to be strongly positive, and he was treated with mercury, still without improvement. October 13, he went to Mount Sinai Hospital, where a diagnosis of exophthalmic goiter was made and medical treatment tried. Shortly afterward he went to the Presbyterian Hospital, where his protein and carbohydrate metabolism was studied by Dr. Geyelin.[25] It was found that the blood sugar was 109 mg. per hundred c.c., the phenolsulphonephthalein output 85 per cent., the leukocytes 11,250, polymorphonuclears 68 per cent., lymphocytes 24 per cent., large mononuclears 5 per cent., and eosinophils 3 per cent. The urine showed traces of sugar, and the Wassermann test was strongly positive.

Physical Examination.—Feb. 11, 1914, the patient is 173.7 cm. tall, of rather large frame with small hands and tapering fingers. The skin is dark, flushed, warm and slightly cyanotic. The beard is thick, the pubic hair normal but the hair on the chest scant and the breasts fatter than the rest of the body. The face is broad and flat, the expression angry and the eyes staring with slight protrusion. The upper lid covers about 2 mm. of the cornea, but does not follow the cornea when the patient looks down. There is some weakness of convergence; he winks but seldom, and the forehead wrinkles but slightly.

There is moderate soft enlargement of the thyroid, especially the right lobe. The neck measures 37 cm. in circumference. The apex of the heart is in the fifth space 11 cm. to the left of the midline, and the limit of dulness 12.5 cm. to the left. The action is rapid and shows a marked irregularity, apparently respiratory in type, with long pauses at the end of expiration. There is a soft systolic murmur at the apex. Carotid pulse is large, radial small. The hands show red areas on the thenar and hypothenar eminences, and there is a tremor when he is excited. There is a scar of an old left inguinal hernia operation, and the left testis is very small and soft; the right testis is large, but of normal consistency. His disposition is nervous, he is excitable, quick in thought and action, and he takes malicious pleasure in teasing his fellow patients, a cretin and a pituitary patient, both somewhat slow mentally.

Treatment and Course.—The data concerning the food and urine are given in Table 2. In February and March the temperature was between 98.4 and 100, the pulse 110-140, the respirations from 26 to 28. March 18, the patient had an acute follicular tonsillitis with a transient rise in temperature to 103.2. Two days later it was normal. During April the temperature was below 99.6, the pulse 104-124, respirations from 20 to 22. Blood pressure, February 15, systolic, 150, diastolic, 70; March 7, 130-60; April 6, 132-82; April 23, 148-74. Beebe's serum was begun, March 5, and the doses slightly increased from time to time. The patient received twenty-three doses up to April 30, and after this the serum was given by Dr. Beebe, himself, at fairly regular intervals. With the serum he was given 1 grain of potassium iodid twice a day. The local reaction from the injection was at times quite marked, but the patient felt so much better that he cheerfully submitted to the discomfort and was enthusiastic about the treatment.

During his stay in the hospital he averaged about three stools a day. He improved distinctly even before he received any treatment other than rest in bed and good food. The diarrhea stopped, as did the sweating, and he was not so nervous. There was slight glycosuria after 100 gm. of glucose. A note, April 15, says he weighed more than on admission, that he was eating more and was feeling stronger each day. It was noticed that he had a polyuria,

25. Geyelin, H. R.: The Carbohydrate Metabolism in Hyperthyroidism as Determined by Examination of Blood and Urine, THE ARCHIVES INT. MED., 1915, xvi, 975.

TABLE 2.—Clinical Data in Case 1

Date	Temperature		Total Calories Food	Carb., Gm.	Fat, Gm.	Food N.	Urine N.	Body Weight	Urine, Volume, c.c.
	Max.	Min.							
2/13 14	99.6	98.6	2,974	176.0	179.0	15.7	14.88	.....	2,735
2/14/14	99.6	98.6	3,675	232.0	234.0	21.3	13.87	62.24	2,500
2 15/14	99.6	98.6	4,091	256.0	252.0	21.5	14.58	62.00	2,450
2 16 14	99.4	98.2	3,662	230.0	238.0	19.7	12.69	61.76	2,525
2 17 14	99.0	98.6	4,324	289.0	273.0	23.3	18.15	61.89	3,150
2/18/14	100.0	98.6	3,971	313.0	228.0	18.0	15.75	62.02	3,720
2 19 14	99.6	98.6	3,970	273.0	259.0	21.8	19.25	61.81	2,720
2/20/14	99.6	98.6	3,620	299.0	201.0	20.0	17.17	61.60	3,240
2/21/14	99.0	98.6	3,801	367.0	198.0	17.6	15.58	62.26	3,045
2 22/14	99.8	98.8	3,758	289.0	216.0	21.6	18.16	62.27	3,830
2/23 14	99.6	99.0	3,874	292.0	226.0	22.6	16.19	62.28	3,240
2/24 14	99.6	99.0	3,628	274.0	212.0	21.0	17.46	61.77	3,200
2/25/14	99.8	99.2	2,411	187.0	119.0	20.9	19.91	61.17	2,890
2/26 14	99.4	98.6	4,246	310.0	232.0	22.7	17.73	61.03	2,360
2/77/14	100.0	98.6	2,533	263.0	121.0	13.0	17.36	60.90	2,990
2 28 14	99.2	98.4	3,520	271.0	205.0	19.8	14.37	60.71	2,610
3/ 1/14	99.2	98.8	3,399	284.0	184.9	20.0	15.60	60.71	3,320
3 2/14	99.6	98.4	2,809	199.0	157.0	20.0	18.21*	60.52	3,240
3/ 3/14	99.8	98.6	3,739	290.0	215.0	21.4	18.21*	60.29	3,150
4/ 4/14	99.8	99.0	2,842	211.0	169.0	15.7	14.59*	60.06	2,375
3/ 5 14	99.8	98.6	3,396	255.0	199.0	19.6	17.15*	60.10	2,930
3/ 6 14	99.6	99.0	3,796	273.0	207.0	20.2	12.61*	60.10	2,000
3/ 7/14	99.8	98.8	.....	.....	.....	....	.....	60.14	.....
3/22 14	99.0	98.0	.....	.....	.....	....	.....	.....	.....
3/23/14	99.4	98.8	2,328	193.0	121.0	16.0	12.16	59.25	3,136
3/24/14	99.0	98.2	3,366	252.0	198.0	19.2	10.59	.....	1.940
3 25/14	99.2	98.4	3,475	301.1	187.0	19.5	11.39	.....	3,200
3/26 14	98.4	98.4	3,408	264.0	196.0	19.6	11.27	60.01	2,890
3/27/14	99.2	98.0	3,494	305.0	187.0	19.1	11.10	60.06	2,490
3/28/14	98.4	98.4	3,640	294.0	206.0	20.0	12.36	60.12	2,960
3/29/14	98.8	98.2	3,891	333.0	214.0	20.9	11.54	60.56	3,365
3/30/14	98.8	98.4	3,560	368.0	164.0	20.4	11.32	61.00	3,460
3 31 14	99.2	98.6	3,976	393.0	195.0	21.5	13.04	61.18	2,500
4/ 1/14	99.6	98.6	4,294	437.0	213.0	20.2	12.11	61.37	2,390
4/ 2/14	98.6	98.0	4,216	422.0	212.0	20.0	12.19	61.88	2,600
4/ 3/14	98.8	98.6	4,232	419.0	215.0	20.2	11.60	61.88	2,900
4/ 4/14	99.6	98.4	4,205	405.0	217.0	20.6	11.85	61.91	2,320
4/ 5/14	99.4	98.4	4,444	435.0	225.0	21.8	12.53	62.26	2,970

* Average feces N. per day March 2 to 6, 3.67 gm.

TABLE 2.—(*Continued*)

Date	Temperature		Total Calories	Carb., Gm.	Fat, Gm.	Food N.	Urine, N.	Body Weight	Urine, Volume, c.c.
	Max.	Min.							
4/ 6/14	99.2	98.4	3,316	379.0	144.0	16.3	13.10	62.26	2,790
4/ 7/14	98.4	98.4	4,529	425.0	214.0	20.3	13.09	62.26	3,060
4/ 8/14	99.0	98.4	4,506	433.0	237.0	20.0	12.62	62.62	2,660
4/ 9/14	98.8	98.4	4,345	444.0	214.0	20.7	12.17	62.90	3,190
4/10/14	98.8	98.4	4,538	424.0	242.0	20.2	13.17	63.19	3,200
4/11/14	99.6	98.2	4,062	372.0	216.0	20.0	13.28	63.32	2,500
4/12/14	99.8	98.2	4,568	401.0	253.0	21.6	11.85	63.45	2,330
4/13/14	98.8	98.6	4,801	550.0	213.0	22.0	17.54	63.01	3,770
4/14/14	98.4	98.4	4,103	408.0	213.0	20.9	12.55	62.58	1,420
4/15/14	98.4	98.4	4,232	406.0	219.0	20.6	15.58	62.92	1,390
4/16/14	99.6	98.4	4,136	388.0	217.0	20.0	15.64	63.26	1,500
4/17/14	99.6	98.8	4,164	343.0	241.0	20.1	15.02	63.58	1,330
4/18/14	99.2	98.4	4,319	355.0	249.0	21.1	15.36	63.58	1,660
4/19/14	99.4	98.8	4,108	380.0	217.0	20.8	14.85	63.58	1,580
4/20/14	99.0	98.8	3,981	350.0	217.0	20.6	15.69	63.90	1,860
4/21/14	99.2	98.4	3,817	319.0	214.0	20.2	14.18	63.81	1,600
4/22/14	99.6	98.6	4,041	369.0	214.0	20.8	17.23	63.73	1,800
4/23/14	98.8	98.4	4,353	399.0	230.0	22.6	17.85	.....	1,980
4/24/14	98.6	98.0	2,943	280.0	151.0	15.1	14.27	63.29	1,889
4/25/14	99.0	98.6	4,064	375.0	214.0	20.7	14.40	.....	1,620
4/26/14	99.4	98.2	4,071	369.0	217.0	20.9	15.52	.....	1,840
4/27/14	99.2	98.2	4,107	361.0	215.0	20.9	15.19	64.56	1,850
4/28/14	98.8	98.2	3,997	360.0	214.0	20.6	14.55	.....	2,360

and the salt in the diet was cut down to from 3 to 4 gm. a day. Two days after this change the urine volume rose to 3,900 c.c., with 22 gm. sodium chlorid in twenty-four hours. After this the volume dropped markedly. By April 24 he was able to be up and about most of the day without fatigue. When he left the hospital the thyroid gland and the eyes were as on admission, but the heart action was regular most of the time.

A year later, April 22, 1915, he spent another day in the metabolism ward and went into the calorimeter again. He had done very well under Dr. Beebe's treatment, gaining 22 pounds in weight. He was able to work in his store eight or ten hours a day, and a few weeks ago walked 5 miles. He seldom has palpitation, but does not try to walk upstairs. He is not so excitable as a year ago. He is able to wear a collar one size smaller than last year. He looks much fatter and stronger, but the eye symptoms are unchanged and the skin is still moist and warm. The apex of the heart is maximum in the fifth space 13.3 cm. to the left of the midline, and the action is so markedly irregular as to suggest auricular fibrillation, a diagnosis which is confirmed by the electrocardiogram.

CASE 2.—*History.*—Edwin T., aged 20 years, student, admitted Feb. 24, 1915, discharged May 1. At the age of 10 had an attack of acute rheumatic fever, and since then has had many sore throats. Three years ago he worked

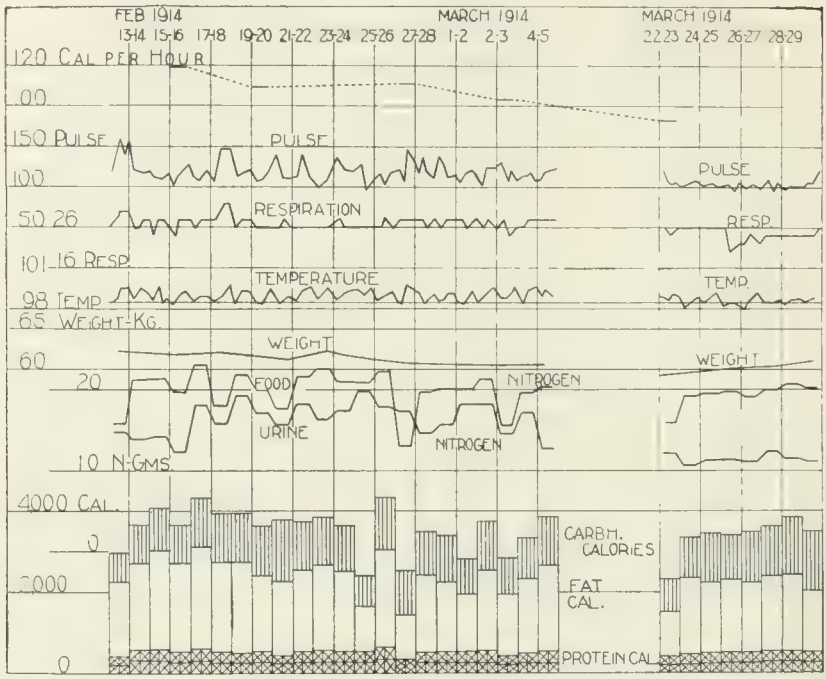

Fig. 1.—Chart in Case 1. Max W.

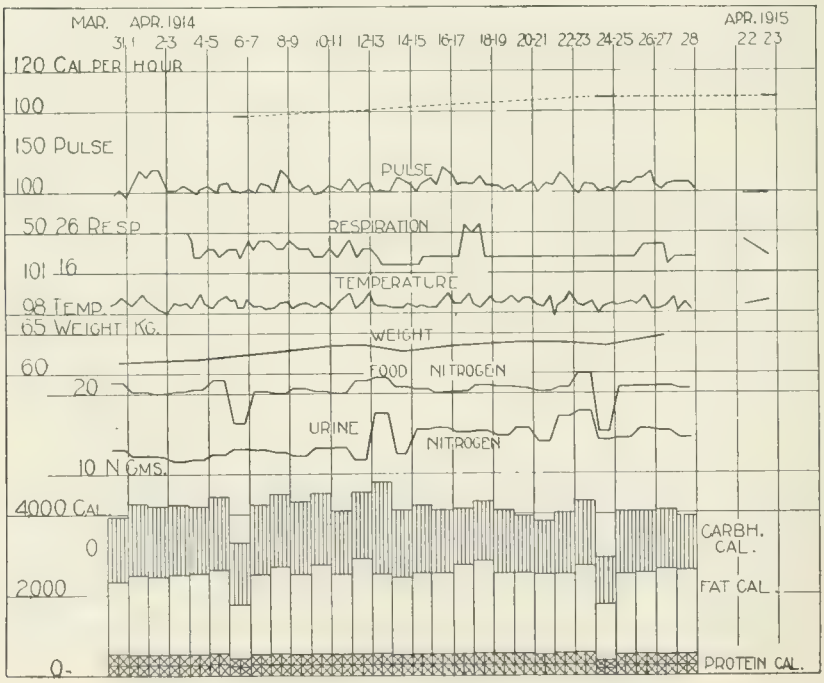

Fig. 2.—Chart in Case 1. Marx W. (continued).

very hard in school. At this time he was able to participate in track athletics. He has been accustomed to taking about six cups of strong tea every day, and has always been nervous. About six months ago he became excitable and restless and a little later was obliged to stop work. About three months ago his friends began to speak of a change in his facial expression. He grew steadily worse until three weeks ago, when a diagnosis of hyperthyroidism was made by Dr. R. J. Shea, and proper treatment started. He lost 13 pounds in weight, but regained most of it under Dr. Shea's care.

Physical Examination.—The patient is 168 cm. tall, moderately thin, the bones are slender, and the distribution of hair is normal for his age. The facies is neurotic in type and the expression angry with slight protrusio bulbi. The tonsils are large and succulent with deep crypts. The thyroid is soft and enlarged, measuring 12 cm. broad, 3 cm. in the vertical direction at the isthmus and 4 cm. at each lobe. The heart is not enlarged, but the first sound is of poor quality, short and sharp, and there is a murmur over the pulmonic area which resembles a hemic or extracardiac murmur. The heart action is forcible, but the radial pulse small. The skin is flushed, warm and moist, often breaking out into sweat. There is a tremor when he is excited.

Treatment and Course.—The first month in the hospital he was given no medication but kept quiet in bed. He became less and less excitable, the skin became cooler and drier and he was happy and helpful in the ward. About March 10 he began to be homesick and at times excitable. March 23, Beebe's serum was started in 5 minim doses almost every day. March 29, there was a severe local reaction accompanied by nausea. After this the serum was given in smaller doses every three days until April 14.

The patient felt a little better after the first few doses of serum, but later grew steadily worse, becoming more depressed, discouraged and at times very nervous. Between April 7 and 21 he was much excited over some personal matters, and was hard to manage. April 21, he was removed to the surgical ward, and the right inferior thyroid artery tied under novocain anesthesia by Dr. Rogers. April 23 and 29, the other three arteries were tied, the patient experiencing no pain, and scarcely ever showing a pulse rate above 100. He felt better and was up and about the ward the day after each operation.

May 10, he was readmitted for a calorimeter observation after ten days in the country. He has felt better and has slept well. The wounds are healing well and his general condition seems improved, but the physical examination is much the same as when first admitted to the hospital. For clinical data see Table 3.

Case 3.—*History.*—James McE., aged 29, factory worker, admitted March 1, 1915, on the service of Dr. Lockwood, with the diagnosis of exophthalmic goiter and alcoholism; at the age of 22 had an attack of appendicitis. He is a heavy smoker, drinks much tea and has periodic attacks of drunkenness lasting about a week. He has been thin, nervous and in rather poor health for the last nine years, and has been very excitable for two or three years. Seven months ago he became very nervous. Five months ago he noticed swelling of the neck, palpitation and dyspnea. At this time he had severe pains in his face not relieved by the extraction of a tooth. Two weeks ago he began to have night sweats, cough, pain in the bones, hoarseness and he lost weight rapidly.

Physical Examination.—The patient is 166 cm. tall, emaciated, restless, expression staring, skin flushed, warm and sweating, pubic and axillary hair scant. Exophthalmos moderate, von Graefe's and Moebius' signs positive. The teeth show much caries and pyorrhea. There is a marked bilateral enlargement of the thyroid gland. Thorax is poorly formed, heart apex 13 cm. to left of midline, regular but markedly overacting, with a rough systolic murmur, loudest to the left of the sternum. Pulse is Corrigan in type. There is a fine tremor of fingers and tongue, and a distinct odor of acetone on the breath.

TABLE 3.—Clinical Data in Case 2

Date, 1915	Food					Urine					
	Total Calories	Protein, Gm.	Fat, Gm.	Carbohyd., Gm.	Food N	Urine N	Excreta N, Gm. †	N Balance, Gm.	Urine Glucose, Gm.	Urine Vol., c.c.	Body Weight, Kg.
Feb. 25-26	3,107	98.7	166.7	280.9	15.79	.....	.....	.....	.....	.....	50.18
Feb. 26-27	2,330*	61.7	134.0	202.7	9.87	15.69	16.68	—6.81	.....	830	49.78
Feb. 27-28	2,882	92.9	139.9	292.6	14.86	16.70	18.18	—3.32	.....	990	.....
Feb. 28- 1	2,723	87.0	142.3	254.7	13.92	17.71	19.10	—5.18	.....	1,030	49.88
Mar. 1- 2	3,704*	101.0	211.6	322.4	16.16	18.44	20.05	—3.89	.....	1,040	.....
Mar. 2- 3	3,462	98.6	184.3	327.9	15.78	16.98	18.56	—2.78	.....	990	.....
Mar. 3- 4	364.1	104.6	188.6	355.6	16.73	17.50	19.17	—2.54	.....	1,065	49.78
Mar. 4- 5	3,221	93.2	172.9	279.3	14.91	16.42	17.91	—3.00	10.64	1,050	49.40
Mar. 5- 6	2,897	132.1	125.9	288.9	22.16	19.51	21.73	+0.43	14.71	1,602	50.42
Mar. 6- 7	2,763	85.5	141.1	268.3	13.68	18.15	19.52	—5.84	15.15	1,595	50.04
Mar. 7- 8	3,760	111.0	210.2	331.6	17.76	15.55	17.33	+0.43	5.31	1,035	50.37
Mar. 8- 9	2,999	155.9	172.9	183.3	24.94	21.22	23.71	+1.23	7.92	1,627	50.06
Mar. 9-10	3,517	105.8	194.6	311.2	16.92	6.87	8.56	+8.36	0	900	50.36
Mar. 10-11	2,419	69.1	124.6	238.9	11.06	13.59	14.70	—3.64	18.06	1,018	49.32
Mar. 11-12	3,549	100.1	203.8	302.5	16.01	15.13	16.73	—0.71	7.20	1,320	.....
Mar. 12-13	3,525	97.1	204.1	299.8	15.53	11.35	12.90	+2.63	7.41	1,075	50.05
Mar. 13-14	3,728	99.5	221.8	306.7	15.92	14.68	16.27	—0.35	9.54	1,160	50.18
Mar. 14-15	3,638	97.6	199.1	338.4	15.61	15.24	16.80	—1.19	7.80	1,260	50.10
Mar. 15-16	2,075	66.9	194.5	242.3	10.70	11.80	12.87	—2.17	5.57	880	50.11
Mar. 16-17	3,180	66.5	205.3	243.4	10.64	13.28	14.34	—3.70	6.87	1,170	49.76
Mar. 17-18	3,159	67.9	202.3	243.6	10.86	8.88	9.97	+0.90	4.62	800	50.01
Mar. 18-19	3,200	70.7	203.3	248.3	11.34	12.53	13.66	—2.32	9.37	1,040	.....
Mar. 19-20	3,550	69.8	218.0	301.8	11.16	11.49	12.60	—1.44	11.87	1,090	50.28
Mar. 20-21	3,631	64.9	253.1	246.9	10.38	10.23	11.27	—0.89	8.24	980	50.28
Mar. 21-22	3,467	72.9	209.3	298.7	11.66	12.61	13.78	—2.12	8.96	1,230	50.27
Mar. 22-23	3,281	65.0	226.1	222.2	10.40	12.75	13.79	—3.39	14.52?	946	49.22
Mar. 23-24	3,305	66.1	203.4	278.5	10.58	10.09	11.15	—0.57	8.88	815	49.98
Mar. 24-25	3,466	65.8	225.0	268.9	10.52	9.47	10.52	0.00	6.87	720	50.18
Mar. 25-26	3,591	66.8	227.0	294.1	10.68	9.47	10.54	—0.14	8.00	920	50.24
Mar. 26-27	3,836	66.0	256.2	288.0	10.56	10 03	11.09	—0.53	9.24	880	50.17
Mar. 27-28	3,639	65.6	247.0	261.8	10.50	9.58	10.63	—0.13	3.08	710	49.94
Mar. 28-29	4,194	71.3	269.2	341.0	11.40	10.65	11.79	—0.39	8.13	820	50.00
Mar. 29-30	3,681	81.6	219.1	314.2	13.05	9.72	11.03	+2.02	14.50	930	50.00
Mar. 30-31	3,602	70.2	118.8	302.1	11.23	10.93	12.05	—0.82	24.51	1,040	50.30
Mar. 31- 1	2,922	74.1	162.7	269.6	11.86	11.57	12.76	—0.90	15.90	780	50.30
Apr. 1- 2	3,874	96.1	214.0	363.3	15.38	13.03	14.57	+0.81	11.42	1,100	50.35
Apr. 2- 3	3,866	96.9	200.0	392.5	15.50	12.50	14.05	+1.45	8.20	1,250	50.63

† Urine N plus 10 per cent. of food N.

TABLE 3.—(*Continued*)

Date, 1915	Food					Urine					
	Total Calories	Protein, Gm.	Fat, Gm.	Carbohyd., Gm.	Food N	Urine N	Excreta N, Gm.	N Balance, Gm.	Urine Glucose, Gm.	Urine Vol., c.c.	Body Weight, kg.
Apr. 5- 6	3,549	89.9	192.4	350.2	14.38	10.73	12.17	+2.21	11.30	970	....
Apr. 6- 7	3,871	94.2	195.0	407.5	15.07	10.37	11.88	+3.19	8.61	800	50.90
Apr. 7- 8	3,758	98.9	197.5	369.9	15.82	11.71	13.29	+2.53	7.53	910	50.75
Apr. 8- 9	3,908	99.4	193.6	414.7	15.90	11.49	13.08	+2.82	17.22	980	51.15
Apr. 9-10	3,532	99.2	211.0	283.6	15.87	12.05	13.64	+2.23	9.77	1,260	51.38
Apr. 10-11	3,874	98.6	215.4	357.7	14.79	?	.....	.....	?	?	51.16
Apr. 14-15	4,109	105.2	195.5	453.6	16.83	11.21	12.89	+3.94	15.65	1,120	51.48
Apr. 15-16	3,303	83.5	195.6	278.6	13.36	11.04	12.38	+0.98	17.0	1,160	.....
Apr. 16-17	3,863	88.4	221.4	351.7	14.14	11.66	13.07	+1.07	14.9	1,390	51.40
Apr. 17-18	3,392	99.6	163.2	157.6	15.94	11.77	13.36	+2.58	.....	1,185	. . .
Apr. 18-19	3,623	98.5	179.5	378.1	15.76	11.43	13.01	+2.75	.....	960	51.50
Apr. 19-20	3,494	88.5	166.2	386.5	14.16	12.33	13.75	+0.41	16.4	1,040	51.40
Apr. 20-21	3,769	98.0	181.8	408.8	15.68	12.55	14.12	+1.56	.....	1,050	51.38

* Food approximate on these two days.

Treatment and Course.—For the first twelve days in the hospital he was kept in bed without medication and improved slowly. March 14, after the first observation in the calorimeter, the Forcheimer ergotin and quinin hydrobromate treatment was begun. He continued to improve slowly in general condition, and gained 6 pounds in weight. The blood pressure was 130-65 and 146-66 mm. Hg. The Wassermann reaction was weakly positive; the urine contained a trace of albumin and a few casts. Temperature 99-100, pulse 108-124 up to March 15, then 82-100.

April 8, he was transferred to the surgical wards, and one superior thyroid artery was ligated under local anesthesia. May 2, one inferior thyroid artery was exposed, but the pulse became so rapid and feeble that the wound was hastily sutured without an attempt being made to ligate the vessel. The patient continued to improve slowly. May 14, the left limit of cardiac dulness was 11 cm. to the left of the midline; the murmur was unchanged. The general condition was better than a month before. For clinical data see Table 4.

Notice of his death in February, 1916, has just been received.

CASE 4.—*History.*—Dr. G. S. L., aged 52, physician, had typhoid fever twenty-five years ago. He smoked from six to nine cigars a day. His eyes have always been prominent. Three or four years ago when his weight was about 215 pounds, he noticed a slight tremor of the hands and slight dyspnea and palpitation on exertion. About one year ago the neck increased in size. The four thyroid arteries were ligated in January, 1914, (three months ago), but he was nearly exsanguinated by a secondary hemorrhage from the superior thyroid artery. He was given quinin hydrobromate for a month, but developed cinchonism. Thyroidectin in September made him worse. For the last week he has had no treatment.

Physical Examination.—April 9, the patient is 180 cm. in height, tall and large framed. The expression is staring, the skin flushed, warm, moist, smooth, and slightly darkened. Dermatographia is present. There is no hair on the chest. There is moderate protrusio bulbi, slight von Graefe's sign, convergence

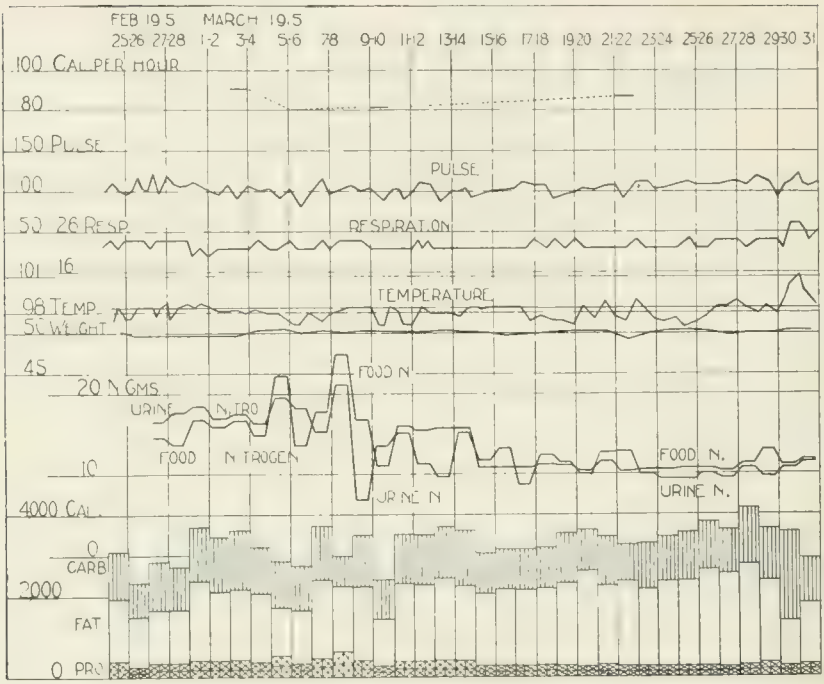

Fig. 3.—Chart in Case 2. Edwin T.

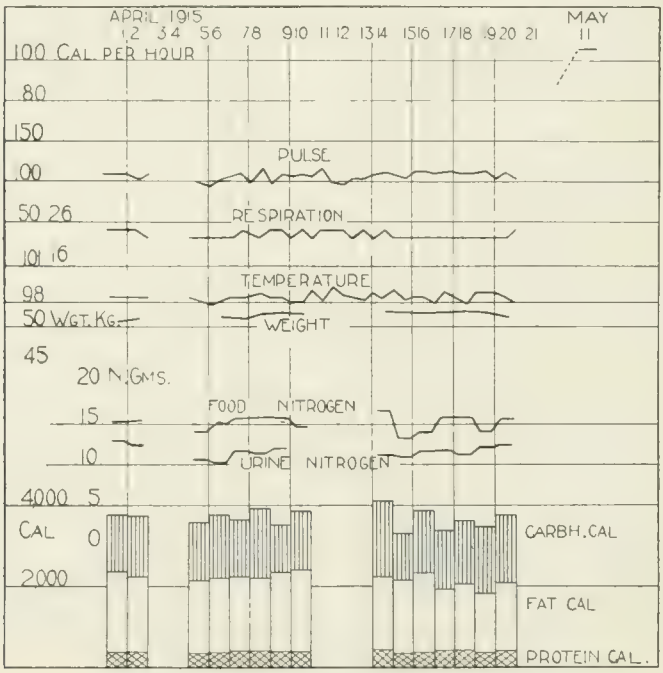

Fig. 4.—Chart in Case 2. Edwin T. (continued)

weak, thyroid lobes and isthmus enlarged. Heart apex impulse is 16 cm. from midline, action regular and heaving. There is a soft systolic murmur maximum in the pulmonic region. Pulse is 100, of large size. Blood pressure is 148 mm. There is a marked tremor of the hands and tongue and also of the legs when standing.

Treatment and Course.—After the calorimeter observation, April 9, the patient was given Dr. Rogers' thyroid "residue," 1 c.c., twice a day until April 16, when he returned for another test, his condition being unchanged except that the heart action was perhaps a little quieter.

In October, 1914, a thyroidectomy was performed. The day after the operation the temperature rose to 101, the pulse to 150, and the respirations to 70 per minute. He died a week later.

TABLE 4.—Clinical Data in Case 3

Date, 1915	Food					Urine					
	Total Calories	Protein, Gm.	Fat, Gm.	Carbohyd., Gm.	Food N	Urine N	Excreta N, Gm. †	N Balance, Gm.	Urine Glucose, Gm.	Urine Vol., c.c.	Body Weight, Kg.
Mar. 9-10	3,322	100.7	183.0	294.5	16.11	11.94	13.55	+2.56	0	1,470	41.39
Mar. 10-11	3,315	94.1	178.7	309.1	15.06	13.51	15.02	+0.04	0	1,380	41.84
Mar. 11-12	3,189	93.7	182.5	270.3	15.00	14.18	15.68	−0.68	0	1,695	41.26
Mar. 12-13	2,558	86.2	145.9	206.9	12.79	15.09	16.47	−2.68	0	1,390	41.16

† Urine N plus 10 per cent. of food N.

Case 5.—*History.*—Peter N., aged 23, with atypical exophthalmic goiter (?), mechanic, admitted April 9, 1915, discharged April 25. His father is 6 feet 4 inches tall (193 cm.). The patient has had sore throat several times. He grew very fast between the ages of 15 and 18. At the age of 18 he became weak and nervous, losing his temper easily. He suffered from severe headaches two or three times a week and his hands grew so tremulous that he has been unable to work for the last year. About a year ago he was in the Massachusetts General Hospital, where his respiratory metabolism was studied by Dr. Means and found to be within normal limits. The superior thyroid arteries were tied, and since then the headaches have been less frequent and the hands drier. He is not much stronger, and he sleeps only two or three hours a night.

Physical Examination.—April 25, 1915, the patient's height is 6 feet 2 inches (187.7 cm.). He is tall and thin with no suggestion of acromegaly. The hands are tapering. The expression is anxious; there are no eye symptoms. The thyroids are soft and slightly enlarged. The hands and feet are sweating, dermatographia marked. Cardiac dulness extends 12 cm. to the left of the midline. Electrocardiograms show a slight respiratory arrhythmia. There is a marked tremor of the right hand and slight tremor of the left. Roentgenoscopy reveals a normal sella turcica. There is a trace of glucose in the urine. During his short stay in the hospital there was no change in his condition. For clinical data see Table 5.

Case 6.—*History.*—Anna K., aged 26, single, born in Ireland, nurse, admitted April 27, 1914, whose mother, one brother and one sister are nervous, had acute rheumatic fever at 16 and has had one attack of severe tonsillitis. For the last ten years she has been high-strung and easily frightened. For several years she has had dyspnea and palpitation on exertion. About December, 1913, all of these symptoms grew worse, and she began to have severe headaches, scanty menses, marked sweating and polyphagia and polydipsia. In February, 1914, she was badly frightened in a runaway, and the symptoms increased in severity. She has lost 15 pounds in weight.

For the last two months she has been given thyroid "residue" by Dr. Rogers. April 4, both superior arteries were ligated by Dr. Rogers in Bellevue Hospital.

Physical Examination.—The patient is very thin, frame small, expression tired and neurotic, speech jerky and agitated, voice weak. Skin moist. Exophthalmos slight, eyelids puffy, no von Graefe's sign, tongue and hands tremulous. Thyroid moderately enlarged, especially on the right. Cardiac impulse diffuse, maximum in the fifth space 8.5 cm. to the left of the midline. Action rapid and regular.

Treatment and Course.—After the first calorimeter observation, the two inferior thyroid arteries were ligated, April 29. May 13, the patient returned to the calorimeter room for the day feeling less nervous and more ambitious than before. June 22, she reported to Dr. Rogers weighing 112 pounds, pulse 90, general condition much improved.

TABLE 5.—Clinical Data in Case 5

Date, 1915	Food					Urine					
	Total Calories	Protein, Gm.	Fat, Gm.	Carbohyd., Gm.	Food N	Urine N	Excreta N, Gm. †	N Balance, Gm.	Urine Glucose, Gm.	Urine Vol., c.c.	Body Weight, Kg.
Apr. 10-11	3,362	85.3	205.4	268.8	13.64	.....	.....	.....	.....	.....	63.95
Apr. 14-15	2,330	66.2	137.4	190.5	10.69	12.17	13.23	—2.64	Slight trace	747	63.44
Apr. 15-16	2,893	69.5	170.2	250.1	11.12	12.16	13.27	—2.15	Trace	840	64.00
Apr. 17-18	2,942	87.3	160.6	265.8	13.97	13.34	14.74	—0.87	.....	1,100	.....
Apr. 18-19	2,757	78.2	143.1	274.6	11.71	11.94	13.11	—1.40	.....	1,240	65.18
Apr. 19-20	2,808	72.7	130.5	316.1	11.63	11.94	12.65	—1.02	Trace	1,080	64.64
Apr. 20-21	3,023	74.7	171.6	273.4	11.95	11.49	12.69	—0.74	.....	1,460	65.28
Apr. 21-22	2,714	83.3	149.5	239.6	13.32	11.82	13.13	+0.19	Trace	1,420	64.65
Apr. 22-23	2,465	84.9	137.8	203.7	13.58	12.95	14.31	—0.73	Trace	1,300	64.32
Apr. 23-24	3,006	85.6	189.3	218.1	13.70	12.81	14.18	—1.37	Heavy trace	1,000	64.20
Apr. 24-25	2,847	87.3	174.6	210.9	13.97	12.61	14.01	—0.04	5.21	1,300	64.45

† Urine N plus 10 per cent. of food N.

Case 7.—*History.*—Anna R., aged 29, unmarried, cook and saleswoman, born in Ireland, admitted May 8, 1913, discharged June 5, five years ago had typhoid fever and shortly afterward noticed swelling of her throat. A year or so later her tonsils were removed by a doctor who told her she had a goiter. Since the attack of typhoid she has had at times tremor, palpitation, restlessness and loss of weight. She thinks she has improved during the last two years. A year or so ago her friends noticed that her eyes were staring. She has been able to work up to the time of admission.

Physical Examination.—The patient is tall and thin, exophthalmos present, von Graefe's and Stellwag's signs present. There is slight tremor of hands and tongue. The heart is slightly enlarged, first sound of poor quality. The thyroid is moderately enlarged.

Treatment and Course.—May 8 to 11 temperature is normal, pulse from 84 to 88, respiration from 20 to 22. The first calorimeter observation was on May 10. On the 12th under local anesthesia Dr. Rogers ligated the left superior and right inferior thyroid arteries and removed the tip of the left upper pole. May 16, the two other vessels were ligated and the tip of the right pole removed. After the first operation the temperature was 99 to 100, pulse 100-112, respiration 24 to 26. After the second operation she was given half a grain of the

Loomis Laboratory special thyroid extract every four hours until May 18. She menstruated from May 16 to May 19. For three days after the operation the temperature was 99 to 102, pulse 96-130, respiration 24 to 32. By May 20, at the time of the second calorimeter observation, the temperature was almost normal. By May 25 she was up and about the ward.

After leaving the hospital she spent two months in the country and gained weight up to 117 pounds. Since then she has been at work and has lost 2 pounds, but has not felt nervous except when she works hard. May 14, 1914, she returned for a calorimeter observation. The scars of the operation were well healed, the left lobe and isthmus of the gland were moderately enlarged and the right lobe considerably enlarged. She was still thin and nervous, and the voice weak and husky, but she looked a little better than a year ago.

A week or so after the last calorimeter observation she was married, and did well until her husband lost his job on account of the war. She started work in the store again, and her weight dropped to 104 pounds and all the symptoms returned. In March, 1915, she reported at the ward very thin, very nervous, hands very tremulous, skin moist, pulse very rapid and small.

Case 8.—*History.*—Sarah M., aged 29, chambermaid, unmarried, born in Ireland, admitted April 29, 1914, discharged May 4, nine years ago came to America, and eight years ago began to suffer from loss of weight, nervousness, weakness, tremor and enlargement of the neck. Three months later she was operated on, and apparently part of the thyroid gland removed. She recovered quickly, and for the next six years enjoyed good health. One year ago she began to have a return of the weakness, nervousness and loss of weight. She became excitable, sweated easily, and slept poorly. At times she had palpitation. She thinks the neck has swollen again.

Physical Examination.—April 29, the patient is tall, fairly well nourished, and does not look sick. The eyes are a little brighter than normal, but there is no exophthalmos, no von Graefe's sign and only slight weakness of convergence. The left lobe of the thymus is absent, the right lobe moderately enlarged. There is slight tremor of the tongue and hands on excitement. The heart is not enlarged and is not overacting; pulse from 86 to 97. The skin is a little moist and not flushed.

Treatment and Course.—The afternoon of the calorimeter observation a partial thyroidectomy was performed by Dr. Rogers. She made a rapid recovery, and when she reported in February, 1915, she had no subjective or objective symptoms.

Case 9.—*History.*—Marion B., aged 22, unmarried, admitted Feb. 4, 1915, discharged February 5, was sent down from the Presbyterian Hospital, where her case was studied in detail by Dr. Geyelin. In 1912 the heart began to beat fast, she sweated easily and began to notice swelling of the neck. Four operations were performed at the Presbyterian Hospital. In July, 1913, two arteries were ligated. Two months later the right lobe of the gland was removed. In February, 1914, an appendectomy was necessary. In July, 1914, part of the left lobe of the thyroid was removed, and she felt better until September, 1914, when her nervousness returned. At the time of her admission she had been menstruating four days.

Physical Examination.—The patient is short and rather stout; excitable. She has a nervous, staring, angry expression. The exophthalmos is marked, the pupils are dilated, the skin moist, the pulse small and soft.

Case 10.—*History.*—Margaret L., aged 51, married, with atypical exophthalmic goiter, auricular fibrillation and mitral insufficiency, admitted March 25, 1914, died May 19, 1914. She had three children in good health. A year ago she began to feel nervous, and lost appetite and weight. She noticed a rapidly growing swelling on the right side of the neck. This was removed by operation in July, 1913. Since then she has been worse and has violent palpitation of the

heart all the time. A month ago she began to have huskiness of the voice, swollen arms and legs and much dyspnea.

Physical Examination.—The patient is well developed and well nourished, dull mentally, slow of speech, the voice husky but not brassy. Skin thick, hard, dry, feels myxedematous. Slight exophthalmos, no von Graefe or Stellwagon sign.

Fig. 5 (Case 12).—Benny L. Cretin holding ruler marked in inches.

Right lobe of thyroid absent, left lobe slightly enlarged. Heart much enlarged with an irregularity shown by tracings to be due to fibrillation. There is a systolic murmur at the apex. There is some fluid in the right pleural cavity. She is dyspneic and looks seriously ill.

Treatment and Course.—At first she was given thyroid "residue," but for three weeks before the calorimeter observation received no medication except codein and ammonium carbonate to control the cough. May 5, a small thymus gland was removed. Histologic examination showed "fatty infiltration of the thymus, thymic tissue appears normal." After the operation she developed fever, rapid pulse, grew weaker and died. There was no necropsy.

Case 11.—*History.*—Miss B. H., aged 31, trained nurse, admitted April 4, discharged April 20, 1914. In childhood had pertussis, scarlet fever, measles, varioloid, mumps, bronchitis, typhoid fever at 15 years, appendicitis and peritonitis at 20, many attacks of tonsillitis and finally tonsillectomy at 22, and diphtheria at 29. For the last two or three years she has worked very hard as a nurse on difficult cases.

Fig. 6 (Case 12).—Benny L. Cretin, 36 years old (continued).

In 1910 she noticed that the thyroid was enlarged. In August, 1913, while nursing a typhoid patient she began to have severe diarrhea with eighteen movements a day. She vomited continually, the pulse was very rapid, and she was excitable and weak. After prolonged rest these symptoms would clear up enough to allow her to work once more. In January, 1914, the right side of the thyroid became enlarged and painful, nervousness increased and she lost 20 pounds. In February, 1914, the right lobe of the gland was removed. Two days later the voice, which had been clear, dropped to a whisper, and did not return to normal for a year or so. After the thyroidectomy the pulse rate dropped from an average of 140 to 72, and she has had but little palpitation and no sensation of undue

warmth. The nervousness has begun just as bad, and she has diarrhea whenever she takes fats. At the time of admission to Bellevue she was much depressed over the loss of her voice, which she feared was to be permanent.

Physical Examination.—April 4, 1914, the patient is of moderate height (159.2 cm.), thin, looks tired and nervous, at times excitable, but always anxious to cooperate in treatment or observations. There is a very slight exophthalmos, slight widening of the palpebral fissure, eyes bright, no von Graefe's sign. There is no enlargement of the isthmus or remaining lobe. The heart is normal and not rapid. There is no dermatographia but at times there is tremor.

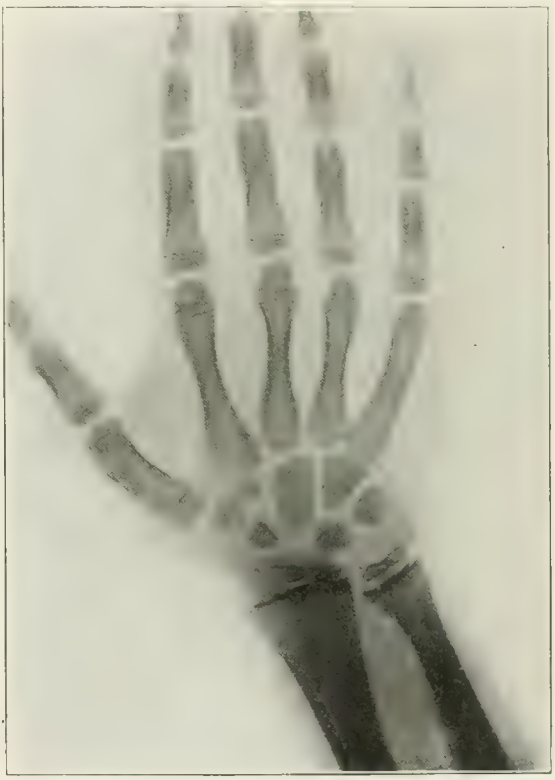

Fig. 7 (Case 12).—Benny L. Roentgenogram of hand.

Treatment and Course.—While in the hospital she was very nervous, slept poorly, and at times vomited. The temperature was normal, pulse 72 to 92, respiration 22 to 26. Until the completion of the second calorimeter observation, April 13, she received no medicine, then thyroid "residue," 1 c.c. hypodermically twice a day until the third test. While in the hospital on a low diet containing about 4 gm. of nitrogen the urinary nitrogen was from 3 to 4 gm. a day.

After leaving the hospital she went to the country, and her appetite improved and she gained strength and did well except for a sudden severe stomatitis which loosened her teeth. In March, 1915, she reported looking thin but almost well. She is able to do light work nursing if she rests between cases. Her physician now attributes many of her symptoms during the past year to hysteria.

Case 12.—*History.*—Benny L., aged 36 (?), with cretinism, Hebrew, admitted April 8, 1914, discharged May 2, was taken to the Children's Hospital on Ran-

dall's Island sixteen years ago, and during that time has had no visitors, so that his previous history is unknown. He has not changed since his admission, and he is very happy playing with the boys and going to school, where he learns practically nothing. He can write his name, dress and feed himself and he corresponds to a child of about 7 years in the Binet test. In 1906 an attempt was made to transplant sheep's thyroid into the pelvis of the left kidney and later into the abdomen. There were no favorable results. He has had numerous courses of treatment with Parke, Davis & Co. thyroid extract, but on doses as small as from one-half to 1 grain three times a day develops tachycardia, weakness and often faints.

TABLE 6.—Clinical Data in Case 12 (Benny L.)

Date	Temperature		Total Calories	Carb., Gm.	Fat, Gm.	Food N.	Urine, N.	Body Weight	Urine, Volume, c.c.
	Min.	Max.							
4/8/14	....	99.2	.....	.....	.....	....	....	....	.....
4/9/14	98.4	98.6	2,381	229.0	120.0	12.5	7.90	.....	1,[illegible]
4/10/14	98.4	98.4	1,118	112.0	53.0	6.6	5.95	23.19	965
4/11/14	98.2	98.2	1,227	125.0	56.0	7.7	6.19	.....	920
4/12/14	98.2	98.2	1,396	140.0	65.0	8.4	6.66	.....	1,000
4/13/14	98.2	98.2	1,496	152.0	70.0	8.7	6.89	.....	1,070
4/14/14	98.6	99.4	1,129	162.0	37.0	4.8	4.67	23.34	795
4/15/14	98.2	98.4	1,360	137.0	63.0	8.2	3.53	.....	710
4/16/14	98.4	99.0	1,229	130.0	55.0	7.3	6.36	.....	950
4/17/14	97.6	98.2	1,034	100.0	51.0	5.9	5.83	24.21	987
4/18/14	97.8	98.0	1,128	109.0	55.0	6.8	5.16	.....	800
4/19/14	98.0	98.6	974	94.0	47.0	5.8	7.01	.....	1,195
4/20/14	98.0	98.2	1,196	117.0	57.0	6.9	6.11	.....	1,195
4/21/14	98.0	98.8	643	66.0	23.0	6.1	5.39	24.06	970
4/22/14	98.0	98.6	1,187	119.0	54.0	7.8	6.19	.....	980
4/23/14	98.0	98.2	704	57.0	38.0	4.4	4.82	24.30	770
4/24/14	97.6	98.0	1,050	103.0	50.0	6.5	5.05	.....	815
4/25/14	97.8	98.6	1,187	135.0	50.0	6.4	5.60	.....	1,040
4/26/14	98.6	98.6	963	103.0	44.0	5.0	4.61	.....	820
4/27/14	98.0	98.6	839	128.0	25.0	3.2	4.13	23.61	672
4/28/14	98.0	98.6	798	68.0	36.0	4.5	4.04	.....	700
4/29/14	98.6	100.0	618	59.0	31.0	3.5	5.32	.....	1,350
4/30/14	99.6	100.2	1,061	99.0	53.0	6.3	6.11	.....	1,400
5/1/14	100.2	101.0	356	37.0	17.0	...	....	23.06	.....

Physical Examination.—The patient (Figs. 5-7) is short, 110.3 cm. tall (3 feet 7½ inches), stout, with prominent abdomen, short, trick extremities and short pudgy hands, the face is broad, wrinkled, with thick lips, broad nose, baggy eyelids, teeth widely spaced, in poor condition with much gingivitis and pyorrhea. The thyroid is not palpable, heart normal, abdomen shows slight umbilical hernia. Scars over right kidney, skin very dry, harsh, inelastic with fine branny desquamation. There are pads of fat on each side of the neck, and others just anterior to axillae. External genitals resemble those of a boy of 7; there are no male secondary sexual characteristics. Blood pressure is 125 mm., Wasser-

mann test strongly positive; the urine contains much sterile pus, evidently due to large calculi shown by roentgenoscopy to be in the pelves of the kidneys. The temperature was slightly subnormal most of the time, pulse 64-80, respiration 18.

The patient was always in good humor. He had a good sense of fun and was a natural clown, his voice was hoarse and childish but he differed from the normal child in being able to sit quiet for hours at a time. He grew tired rather easily, his appetite was very small, his bowels constipated. April 27, in the afternoon, the administration of thyroid extract was begun, 1 grain three times a day; the temperature rose to the level of 100 F, pulse 100, respiration 18, blood pressure 115. He felt limp, and looked sick so that the drug had to be discontinued. For clinical data see Table 6.

Discussion of Results

THE BASAL METABOLISM IN EXOPHTHALMIC GOITER

The determination of the basal metabolism in exophthalmic goiter is a matter of technical difficulty. The patients are excitable, restless and easily tired. For this reason great care must be used when nose or mouthpieces or face masks are employed, since these may prove uncomfortable toward the end of an experiment or series of experiments. The respiration calorimeter, although perfectly comfortable for a normal person for five hours, often tires a goiter patient after three hours. Fortunately the apparatus is so delicate and accurate that the measurement of the heat production by the method of indirect calorimetry is satisfactory after a preliminary period of three-fourths hour. Experiments one hour long could be employed, but two hour observations are more satisfactory since the method of direct calorimetry is not as accurate as could be wished in the first experimental hour. This will be discussed later.

There is a distinct tendency for the patients to become more restless as the observation progresses, and it will be noted that the metabolism in the fasting experiments is usually higher in the second hour than in the first. There is also a tendency on the part of patients as well as normal controls to show a slightly higher metabolism the first time they are the subject of a real experiment, although they are all trained by a short "dummy experiment" a day or so previously. Goiter patients on some days are distinctly more disquieted than usual, and one gets the impression that on such days the increase in metabolism is due partly to the restlessness and partly to an exacerbation of the disease which causes both restlessness and increased heat production.

It has long been realized that tremor and involuntary activity on the part of goiter patients might be responsible for a considerable portion of the increase in metabolism. Magnus-Levy discussed these factors, and found that the increase in metabolism is almost as marked when the patient is sleeping or under the effect of opium. He found also that the tremor of paralysis agitans increased the oxygen consumption only from 20 to 30 per cent. A careful scrutiny of the

results reported in the present work shows that restlessness, tremor and mental irritability contribute only a small percentage of the increase in most of the cases. The activity of the patients was checked by the delicate work-adder and by careful observation. All of the patients

TABLE 7.—The Influence of Sleep, Restlessness, Etc., on Metabolism in Hourly Periods

Subject and Date	Calories per Hour Ind.	Per Cent. above Lowest Figure	Work-Adder Cm.	Behavior of Patient
Case 1 (Max W.) Feb. 16	114.6	..	31	A little restless; involuntary tremor at end of period
	124.1	9	14	A little restless
Feb. 20	104.9	..	16	Calm and quiet
	114.2	9	22	Calm; slightly excited by visitor for ten minutes
Feb. 21	120.8	3	26	After dextrose; quiet
	117.2	..	55	After dextrose; very restless
Mar. 4	101.1	..	15	Asleep the whole hour
	106.2	5	58	Awake, pulse rapid last half hour
April 6	92.2	..	25	Quiet; asleep 50 minutes
	99.4	8	55	Very restless
	101.4	10	51+	Very restless; uncomfortable
April 23, 1915	102.8	..	21	Fairly quiet; asleep 30 minutes
	111.0	8	33	Fairly quiet; asleep 5 minutes
Case 2 (Edwin T.) Mar. 3	93.6	5	23	Quiet, reading 45 minutes
	89.2	..	30	Asleep 50 minutes in 90-minute period
Mar. 6	80.2	0	6	Reading whole hour; very quiet
	80.2	..	19	Asleep 55 minutes; fairly quiet
Mar. 10	75.4	..	16	Sleeping; slightly restless
	87.3	16	18	Reading 55 minutes
Mar. 22	79.8	..	?	Sleeping; very quiet
	88.0	11	10	Reading 55 minutes; quiet
	94.8	20	30	Asleep
May 11	96.2	..	15	Restless; stretched arms
	115.1	20	34	Restless; vomited shortly after exp.
Case 3 (James McE.) Mar. 12	95.8	..	14	Reading quietly 50 minutes
	98.6	3	23	Reading quietly 36 minutes
	101.7	6	30	Not reading; fairly quiet
Mar. 31	88.6	..	10	Reading 60 minutes; quiet
	95.6	8	26	Reading 32 minutes; restless
Case 4 (Dr. G. S. L.) April 16	104.8	..	29	Fairly quiet
	109.3	4	58	Slightly restless
Case 6 (Anna K.) April 28	102.6	1	36	Restless
	101.5	..	38	Quieter

were as quiet as the normal controls for at least some of the periods of observation. Most of them slept quietly during a considerable portion of some periods. When we compare the sleeping and quiet periods with those in which the patient was awake or excited or restless, we find no constant and striking increase large enough to change our inter-

TABLE 8.—Summary of Results of Respiration Experiments

Subject and Date	Character of Experiment	Average Pulse Rate	Average R. Q.	Per Cent. Divergence of Direct from Indirect Calorimetry	Indirect Calorimetry Average Calories per Hour					Per Cent. Rise above Patient's Own Basal Metabolism	Day of Basal Determination Used for Comparison	Remarks
					Per Kg.	Per Sq. M. Mech	Per Cent. Rise above Average Normal Basal 34.7 Mech	Per Sq. M. Linear	Per Cent. Rise above Average Normal Basal 39.7 Linear			
Case 1 (Max W.)												
2/16/14	Basal	137	0.76	— 4	1.93	62.0	+79	69.4	+75	....	.....	Slightly restless
2/18/14	¾ to 3¾ hrs. after 100 dextrose	124	0.90	— 1	1.79	57.7	....	64.7	....	+ 2	Av. Feb. 20, 27, Mar. 4	Slightly restless
2/20/14	Basal	111	0.77	— 4	1.78	57.0	+64	63.7	+60	....	.....	Quiet
2/21/14	¾ to 2¾ hrs. after 100 dextrose	105	0.94	— 5	1.91	61.5	....	68.8	....	+ 9	Av. Feb. 20, 27, Mar. 4	Restless 1 hour
2/25/14	1½ to 3½ hrs. after 8.9 N as casein	138	0.83	— 3	2.02	64.7	....	71.9	....	+14	Av. Feb. 20, 27, Mar. 4	Quiet
2/27/14	Basal	136	0.77	— 2	1.83	58.4	+68	65.4	+65	....	.....	Restless 1 hour
3/ 2/14	1½ to 3½ hrs. after 9.0 N as meat	101	0.82	+ 3	1.87	59.6	....	66.5	....	+ 5	Av. Feb. 20, 27, Mar. 4	Quiet
3/ 4/14	Basal	108	0.77	— 2	1.73	54.9	+58	61.0	+54	....	.....	Asleep 1 hour; restless 1 hour
3/23/14	Basal	87	0.77	+ 4	1.57	49.7	+43	55.3	+39	....	.....	Quiet; dozed
4/ 6/14	Basal	95	0.79	+ 1	1.59	51.0	+47	57.1	+44	....	.....	Restless
4/24/14	Basal	120	0.78	+ 1	1.69	54.4	+57	60.9	+53	....	.....	Restless
4/23/15	Basal 1 yr. later	99	0.77	— 4	1.46	49.6	+43	57.7	+45	....	.....	Quiet; dozed
Case 2 (Edwin T.)												
3/ 3/15	Basal	99	0.78	— 4	1.84	54.9	+58	61.7	+55	....	.....	Slightly restless
3/ 5/15	2 to 6 hrs. after 8.95 N as casein	88	0.86	— 4	1.78	53.4	+54	60.6	+53	+ 7	Av. Mar. 3, 6 and 10	Quiet
3/ 6/15	Basal	87	0.81	+ 4	1.60	47.9	+38	53.8	+37	....	.....	Quiet
3/ 8/15	2 to 5 hrs. after 10.19 N as meat	95	0.82	— 6	1.88	56.2	62	63.4	....	+11	Av. Mar. 3, 6 and 10	Quiet
3/10/15	Basal	92	0.80	—12	1.65	49.1	+42	55.3	+39	....	.....	Quiet
3/22/15	Basal	107	0.79	— 3	1.71	52.8	+52	59.4	+50	....	.....	Quiet
5/11/15	Basal 2 to 3 weeks after ligation	134	0.76	— 4	2.10	63.0	+82	71.2	+79	....	.....	Slightly restless

Case 3 (James McE.)												
3/12/15	Basal	109	0.78	− 6	2.40	67.2	+94	74.4	+87	....	.....	Quiet
3/31/15	Basal after quinin and ergotin	97	0.82	− 4	2.30	64.0	+84	70.7	+78	....	.....	Fairly quiet
5/14/15	Basal after ligation...	115	0.75	− 8	2.30	68.1	+97	76.1	+92	....	.....	Fairly quiet
Case 4 (Dr. G. S. L.)												
4/ 9/14	Basal	100	0.77	− 0	1.45	46.9	+42	55.0	+38	....	.....	Quiet
4/16/14	Basal after thyroid "residue"	99	0.76	− 4	1.54	51.5	+50	57.6	+45	....	.....	Slightly restless
Case 5 (Peter N.)												
4/14/15	Basal	71	0.83	+ 8	1.10	35.5	+ 2	38.8	− 2	....	.....	Very quiet
Case 6 (Anna K.)												
4/28/14	Basal after ligation of 2 arteries	121	0.75	− 5	2.30	66.1	+104	....	....	....	.....	Fairly quiet
5/13/14	Basal after ligation of 2 more arteries	100	0.81	− 8	1.90	55.1	+71	....	....	....	.....	Very quiet
Case 7 (Anna R.)												
5/10/13	Basal	119	0.79	− 8	1.45	43.4	+34					
5/20/13	Basal after ligation...	...	0.76	− 7	1.79	49.9	+55	....	....	....	.....	Quiet
5/28/13	Basal	...	0.77	− 5	1.64	49.2	+52					
5/14/14	Basal 1 yr. later	97	0.80	− 4	1.48	43.6	+35	....	....	....	.....	Very quiet
Case 8 (Sarah M.)												
4/29/14	Basal*	92	0.78	− 4	1.41	43.8	+36	....	....	....	.....	Fairly quiet
Case 9 (Marion B.)												
2/5/15	Basal	127	0.77	− 1	1.40	44.1	36	....	....	....	.....	Restless
Case 10 (Mrs. L.)												
4/20/14	Basal	85	0.76	− 1	1.30	42.0	30					
Case 11 (Miss B. H.)												
4/ 8/14	Basal	60	0.83	+ 4	1.21	35.4	+10	40.0	+ 8	....	.....	Quiet
4/13/14	Basal	74	0.81	− 1	1.19	35.1	+ 9	39.9	+ 8	....	.....	Very quiet
4/18/14	Basal after thyroid "residue"	94	0.84	2	1.15	33.4	+ 3	37.8	+ 2	....	.....	Very quiet
Case 12 (Benny L.)												
4/10/14	Basal	84	0.92	+ 8	1.21	27.6	- 20	35.0	17	....	.....	Very quiet
4/14/14	1 to 4 hrs. after 100 dextrose	88	1.00	1	1.34	31.4	. ..	37.9	....	+ 15	April 10	Very quiet
4/21/14	1½ to 5½ hrs. after 3.6 N casein	82	0.93	+ 6	1.23	28.9	....	34.9	....	+ 13	April 23	Quiet
4/23/14	Basal	78	0.87	− 0	1.09	25.6	26	31.0	22	....	.....	Quiet
4/27/14	1 to 4 hrs. after 70 dextrose	79	0.95	+ 0	1.19	27.7	....	33.3	....	+ 7	April 23	Very quiet
5/ 1/14	After thyroid extract	95	0.79	− 6	1.44	33.2	- 4	39.8	+ 0	+ 28	April 23	Very quiet

* After very small breakfast.

pretation of the results. All of the experiments which show significant differences between the various periods either in the heat-production, work-adder reading or activity of the patient as noted in the protocol have been grouped in Table 7. Some of the patients were allowed to read while in the calorimeter, since it was found that they were quieter if their minds were pleasantly occupied. It will be seen that the metabolism was about the same during the reading periods as during the periods of slightly restless slumber characteristic of this disease. Edwin T. (Case 2) was the only subject who showed an increase of more than 10 per cent. on account of movement. On March 10, reading seemed to increase the calories 16 per cent. March 22, the reading metabolism is about half way between that of two widely varying sleeping periods, and May 11 it rose on account of nausea in the last period.

The results of all the respiration experiments are summarized in Table 8, and the average metabolism on the days of the basal determinations compared to the normal averages discussed in the thirteenth paper of this series. It will be noted that in all the thin patients the rise above the normal is less marked when the measurements are made according to the linear formula than if Meeh's formula for the determination of the surface area be employed. If we confine our attention for the time being to the basal metabolism during the first week that the patients were in the hospital, we can compare the cases here reported with those already described in the literature. In all there is a total of forty-five patients whose respiratory metabolism has been studied, fasting and as quiet as the circumstances would permit. It has seemed best to group these in Table 1 arranging them according to the calories per square meters of surface area as calculated from Meeh's formula. The calculation of the calories has been made from the tables of Magnus-Levy,[26] using the oxygen consumption and respiratory quotient, assuming that protein furnished about 15 per cent. of the calories. This gives a more accurate basis of comparison than the mere statement of cubic centimeters of oxygen or carbon dioxid per kilogram and minute. Still better comparisons might be made if we could use the linear formula or its modification; but this is impossible because many of the authors do not give the heights of the patients. We are similarly handicapped in the tabulation of other symptoms, since many of the clinical reports are very brief. Still it is possible to make a fairly complete chart which allows us to see which symptoms accompany the cases with high metabolism. The plus marks are necessarily my own interpretation of the author's statements.

26. Magnus-Levy: Von Noorden's Handbuch der Pathologie des Stoffwechsels, Ed. 2, 1906, i, 207.

At the head of the list comes Hirschlaff's patient Louise B. shortly before her death with the most extreme symptoms of hyperthyroidism. There are eight other subjects whose metabolism is greater than 56.5 calories per square meter per hour, a figure 75 per cent. above the average for women. Of these all are classified as severe or very severe, except one designated "ziemlich schwer." All show a very rapid pulse, thyroid enlargement, exophthalmos, mental irritability, warmth of skin, tremor and emaciation. Eleven more patients are above the figure which represents a 50 per cent. increase in metabolism. Of these, one is classified as very severe, five are classified as severe, and five as moderately severe. With most of these the pulse rate averages over 100 and there are signs of cardiac enlargement. Goiter, mental irritability, tremor and warmth of skin are present in all. Exophthalmos is absent in one, and the emaciation is slight as a rule.

The figure 38.2 represents the upper normal limit for men, and 35.5 that for women. Between these marks and that indicating a 50 per cent. increase there are sixteen patients, six severe, one moderately severe, four mild, and the others atypical, "forme fruste" or simple goiter. In them the tachycardia is not so marked, and exophthalmos and emaciation are inconstant. Goiter, mental irritability, tremor and warmth of skin are present. There are eight subjects within normal limits. Among these are four mild cases of exophthalmic goiter, two of simple goiter, and two cases in which operation had been performed, one of these being atypical from the start. One patient is below the normal limit. Magnus-Levy in one article classifies her case as half way between Kropf and "forme fruste," and in another article as simple goiter and refers to her as hysterical.

Age is a factor which changes our interpretation of some of the results. The boy M. P., aged 11½ years, with a small struma, is really a little below the average level for his age. Frau B. and Frl. U., aged 52 and 55, respectively, are at an age when the normal metabolism is from 5 to 10 per cent. lower than the average figure for younger women.

The patients whose metabolism is within or below the normal limits show but slight tachycardia, slight if any goiter or exophthalmos and no unusual warmth of skin. Two show mental irritability and tremor.

We must not forget that some of the symptoms of hyperthyroidism are due either wholly or in part to the increased metabolism. The sensation of unusual warmth, the hot, flushed skin and the sweating are caused by the fact that each square centimeter of skin must radiate more heat than in a normal person. These phenomena are found with an increased metabolism from almost any cause, although it is quite possible that in exophthalmic goiter they may be more marked for the same degree of increase. In like manner the loss of

weight is due to the fact that the increased heat production is not balanced by an increased caloric intake and absorption. The appetite of the goiter patient would keep the weight stationary or even cause an increase were the metabolism normal. For some reason the appetite and absorptive powers in hyperthyroidism are not quite sufficient to maintain weight, although laboring men with a much higher caloric requirement per day remain in nutritive equilibrium. This may be accounted for in part by the increased nitrogen metabolism, which is usually ascribed to a toxic destruction of protein. Part of the increase in pulse rate is also due directly to the increased metabolism which necessitates a greater blood flow. This, however, would not account for all of the increase, since muscular work, raising the metabolism from 50 to 100 per cent., seems to increase the pulse rate by only 10 to 30 beats per minute. Still we must remember in discussing the tachycardia and cardiac enlargement that the continued stimulation of metabolism in hyperthyroidism is very different from the stimulation due to muscular exercise which lasts for only a fraction of a day. If it were possible to stimulate the metabolism of a normal man twenty-four hours a day over the period of a year or more, we might perhaps reproduce the cardiac symptoms of hyperthyroidism as well as the warmth of skin and loss of weight.

The more we study the table, the more apparent it becomes that the increase in metabolism is proportional to the severity of the disease. The only exceptions in the group are found in doubtful or atypical cases, or those that have undergone operative treatment. Very severe cases show a metabolism 75 per cent. or more above the average, severe cases 50 per cent. or more, moderately severe and mild cases show an increase of less than 50 per cent., while a few mild and several atypical or cases in which operation has been performed are within normal limits. The degree of tachycardia, goiter, exophthalmos and mental irritability are roughly proportional to the increased heat production. Unfortunately we have not enough data to compare the level of metabolism with the degree of mononucleosis, the sugar tolerance, the drop in blood pressure from large vessels to the periphery, the eye sympoms and many others that are considered of prime importance by various authors.

THE RESPIRATORY QUOTIENTS

In the patients with high basal metabolism, the respiratory quotients are necessarily low after a fast of seventeen hours or more. Most of them are close to the figure of 0.77, which indicates that about 17 per cent. of the calories are derived from the combustion of carbohydrates. With normal men the quotient under similar conditions varies rather widely, but averages 0.82, showing that about 32 per

cent. of the calories are derived from carbohydrates. Therefore goiter patients who are kept in bed in the hospital evidently have less available glycogen after a fast of seventeen hours than normal men who have been up and about during the evening and morning before the experiment. This may be due either to the fact that the thyroid patients have insufficient appetites and start the evening with a smaller store of glycogen, or else that they use up the starch of the food and the stored glycogen more rapidly than the controls. The respiratory quotients here reported give no indication of any qualitative change in the metabolism. The lowest average basal quotient is 0.75, and this is exactly what might be expected in patients with exceedingly high metabolism. In Case 1 (Max W.) the quotients rose to 0.94 on one day and 0.98 on another after the ingestion of 100 gm. of dextrose. The latter figure shows that 89 per cent. of the calories was being derived from carbohydrate from two to three hours after the sugar was taken. The urine passed immediately afterward contained 3.9 gm. glucose, but it is evident that this glycosuria was not due to any impairment of the power to metabolize carbohydrates. The explanation must be sought in an abnormality of mobilization. Cramer and Krause[27] show that after the ingestion of thyroid substance the liver no longer retains glycogen as before.

DIRECT AND INDIRECT CALORIMETRY

One contribution to the science of metabolism which can be made only by a respiration calorimeter is a comparison of the direct and indirect calorimetry. The former method depends on the direct measurement of the heat of radiation, conduction and vaporization. The latter depends on the measurement of carbon dioxid and oxygen and the calculation of the foodstuffs metabolized each hour. It has been shown in the fourth paper of this series that the two methods agree within 0.17 per cent. when normal controls are studied in periods lasting three hours or more. In the seventh paper it was shown that the method of direct calorimetry gave a total which was 2.2 per cent. less than the indirect total in typhoid fever, and that the average divergence of the two methods in the individual experiments was 5 per cent. In the cases of hyperthyroidism here reported, the total number of calories measured is 8,052 according to the indirect method, and 7,823 according to the direct method, which is 2.9 per cent. lower. The individual experiments show that the average divergence is $\pm$ 4.1 per cent. With the cretin Benny L., the direct calorimetry was 1.5 per cent. higher than the indirect. When one considers the technical difficulty of making short respiration chamber experiments on sick patients, the close agreement of two absolutely independent methods is very

27. Cramer and Krause: Proc. Roy. Soc. London, 1913, B., lxxxvi, 550.

striking. The fact that the direct calorimetry is slightly lower can be ascribed to technical errors in the direct method, which have been discussed in previous papers. It may be due to an unmeasured loss of heat to the bed and bed clothing or to an error in the measurement of the average temperature change of the body. The effect of these errors is minimized in long experiments such as are used in normal controls, but it is necessary to use short experiments with patients. The slight disagreement does not point to any disturbance of the intermediary metabolism. The law of the conservation of energy holds good in exophthalmic goiter.

WATER ELIMINATION THROUGH SKIN AND LUNGS

In the thirteenth paper of this series it was shown that under the atmospheric conditions prevailing in the calorimeter experiments, normal men eliminated on an average 28.4 gm. of water an hour through skin and lungs. Of the total calories produced, the average percentage dissipated through vaporization of water was 23.9. Few of the experiments showed a deviation of more than 10 per cent. from this mean.

In hyperthyroidism the heat production and water vaporization are both increased, and in Table 9 we see that they are increased in almost equal proportion. The average water elimination of the severe and moderately severe cases is 39.9 gm. per hour. On an average, 25.7 per cent. of the heat is dissipated through vaporization, or almost the same as in the normal controls. The percentage rise in water elimination through skin and lungs would seem to be a valuable guide as to the extent of the rise in total metabolism.

SPECIFIC DYNAMIC ACTION OF PROTEIN AND DEXTROSE

Owing to the variations in the basal metabolism of goiter patients, the results of this part of the investigation are not as clear cut as might be desired. In Table 10 the figures obtained on Max W. (Case 1), Edwin T. (Case 2) and the little cretin, Benny L. (Case 12) are given. It is difficult to select the proper basis of comparison for these three groups. Should we use the same actual amount of food, the same amount per kilogram, per square meter of body surface or per calories metabolized per hour? Should we compare the results in terms of percentage increase in metabolism or in the terms of extra calories? In the two exophthalmic goiter cases the protein meals produced almost exactly the same percentage rise as in the normal controls. With Max W. (Case 1) the metabolism was higher after the meal containing the protein in the form of casein and egg albumin than after the same amount of protein as found in beef. Edwin T. (Case 2) showed just the opposite, but the meat contained more

TABLE 9.—Water Elimination of Goiter Patients: Basal Experiments

Subject and Date	Average Water, Gm. per Hour	Average Calories per Hour, Dir. Calor.	Per Cent. Calories Lost through Vaporization
Case 1 (Max W.)			
Feb. 16, 1914	45.33	114.40	29.16
Feb. 20, 1914	40.95	105.52	22.67
Feb. 27, 1914	41.48	109.34	22.16
Mar. 4, 1914	42.14	102.06	24.10
Mar. 23, 1914	35.76	96.41	21.66
Apr. 6, 1914	35.37	99.16	20.83
Apr. 24, 1914	37.22	107.22	20.28
Apr. 23, 1914	48.53	102.42	27.68
Average	40.85	.....	23.57
Case 2 (Edwin T.)			
Mar. 3, 1915	43.60	86.98	29.3
Mar. 6, 1915	35.30	83.81	24.6
Mar. 10, 1915	30.94	71.57	25.3
Mar. 22, 1915	37.76	84.82	26.0
May 11, 1915	54.06	101.30	31.2
Average	40.33	.....	27.3
Case 3 (J. McE.)			
Mar. 12, 1915	43.32	92.48	27.4
Mar. 31, 1915	31.59	88.55	20.17
May 14, 1915	57.31	95.75	34.9
Average	44.07	.....	27.49
Case 4 (Dr. G. S. L.)			
Apr. 9, 1914	30.24	103.73	17.03
Apr. 16, 1914	36.83	102.89	20.91
Average	33.54	.....	18.97
Case 5 (Peter N.), Apr. 14, 1915	28.31	74.80	12.37
Case 6 (Anna K.)			
Apr. 28, 1914	51.51	97.05	31.00
May 13, 1914	37.25	77.79	27.97
Average	44.38	.....	29.48
Case 7 (Anna R.)			
May 10, 1913	31.49	62.11	29.61
May 20, 1913	43.29	71.28	18.02
May 28, 1913	41.83	67.50	36.19
May 14, 1914	29.55	68.04	25.36
Average	36.45	.....	27.29
Case 8 (Sarah M.), Apr. 29, 1914	37.48	75.37	16.5
Case 9 (Marion B.), Feb. 5, 1915	35.77	80.16	26.06
Case 10 (Mrs. L.), Apr. 20, 1914	40.51	80.86	29.26
Case 11 (Bessie H.)			
Apr. 8, 1914	26.44	59.41	25.99
Apr. 13, 1914	21.06	56.81	21.65
Apr. 18, 1914	22.71	52.02	25.49
Case 12 (Benny L.)			
Apr. 10, 1914	10.48	29.61	20.67
Apr. 23, 1914	10.90	26.19	24.31
May 1, 1914	11.78	31.00	22.71
Averages Severe Cases—			
Case 1 (Max W.)	40.85	.....	23.57
Case 3 (James McE.)	44.07	.....	27.49
Case 4 (Dr. G. S. L.)	33.54	.....	18.97
Case 6 (Anna K.)	44.38	.....	29.48
Moderately Severe—			
Case 2 (Edwin T.)	40.33	.....	27.3
Case 7 (Anna R.)	36.45	.....	27.29
Average of six cases	39.94	.....	25.7

nitrogen than the casein meal. Max W. (Case 1) showed a somewhat smaller percentage rise in metabolism than the normal controls after 100 gm. dextrose. The findings on the small cretin Benny L. (Case 12) are difficult to interpret on account of his low calorific output, but he seems to show results not far from the normal.

It appears that the specific dynamic action of protein and dextrose is approximately the same as in health. There is certainly no marked increase such as some writers[28] have surmised, and there is no marked decrease such as is found in typhoid fever. There is little difference between protein in the form of meat and in the form of casein and egg albumin.

TABLE 10.—Specific Dynamic Action of Foods in Hyperthyroidism

Subjects	Food	No. of Experiments	Average Gm. N or Dext. in Food	Average Gm. N or Dext. per Kg. of Body Weight	Average Gm. N or Dext. per Cal. per Hour	Average Per Cent. Rise in Metabolism above Subject's Basal
Two normal men....	Protein meal.....	2	10.1	0.149	0.144	9.7
Case 1 (Max W.).....	Casein and meat...	2	8.9	0.146	0.082	9.5
Case 2 (Edw. T.).....	Casein and meat...	2	9.6	0.19	0.12	9.0
Case 12 (Benny L.)†	Protein meal.....	1	3.6	0.15	0.135	13.0
Three normal men...	Glucose*.....	3	100.0	1.37	1.36	9.7
Case 1 (Max W.).....	....	2	100.0	1.64	0.92	5.5
Case 12 (Benny L.)†	.....	1	100.0	4.20	3.7	15.0
Case 12 (Benny L.)†	.....	1	70.0	2.94	2.6	7.0

* Subjects were given 115 gm. commercial glucose, which are equivalent to 100 gm. pure glucose.
† Cretin.

THE EFFECTS OF TREATMENT

Max W. (Case 1), after a stay of four months in various hospitals, was in the Bellevue metabolism ward for five days before the first determination of his basal metabolism. He received no treatment except good food, mental quiet and rest in bed with permission to get up and walk about for a few minutes at a time. In seventeen days the metabolism fell 12 per cent. After this he received the Beebe serum treatment with 1 grain of potassium iodid twice a day. In the next nineteen days the metabolism fell about 9.5 per cent., and the general condition improved correspondingly. Then while the treatment was being continued, the heat production rose almost to its level before the serum was begun. After one whole year of serum injections, during which time he was at home and at work, he returned

28. Von Noorden: New Aspects of Diabetes, New York, E. B. Treat & Co., 1912, p. 20.

to the hospital with a metabolism 5 per cent. lower than the day before treatment was begun. His mental irritability had lessened, his strength had increased, but his heart had developed fibrillation.

Edwin T. (Case 2) first took to bed when he was admitted to the metabolism ward. After a week of absolute rest in bed the first basal test was made. Three days later the metabolism was 13 per cent., and a week later 10 per cent. lower without medication. Subsequently it rose to within 4 per cent. of its original level under the influence of homesickness and some personal worries. He was given serum, but circumstances made it necessary to operate before a calorimeter test could be made. April 21, 23 and 29, all the thyroid arteries were ligated under painless local anesthesia. Twelve days after the last operation, his metabolism was 20 per cent. higher than before. He looked worse, but said he felt stronger.

James McE. (Case 3) was in the hospital twelve days before his first basal test. Immediately after this he was put on the Forcheimer ergotin and quinin hydrobromate treatment. In nineteen days the metabolism fell 5 per cent. April 10, one artery was tied; May 2, an operation was interrupted by collapse on the part of the patient. Twelve days after this the metabolism was 6 per cent. above the lowest point previously measured.

Anna K. (Case 6) was admitted to Bellevue April 27 and placed in the calorimeter the next day. On the 29th two thyroid arteries were ligated. Two weeks later the metabolism had fallen 17 per cent., which is about the decrease usually found during the first two weeks a patient is at rest in a hospital.

The basal metabolism of Anna R. (Case 7) was measured the third day she was in the hospital, May 12. On that afternoon, and May 16, the four thyroid arteries were tied. Four days later the metabolism was 15 per cent. above its original point, and eight days later it had changed but little. One year later it was at its original level.

The thyroid extract called thyroid "residue" had but slight effect on the metabolism. With Dr. G. S. L. (Case 4), a severe case, the metabolism rose slightly, with Miss B. H. (Case 11) it fell.

OBSERVATIONS ON A CRETIN

The basal metabolism of Benny L. (Case 12) averaged about 20 per cent. below the normal for adults according to his measured surface area. Children of his size average about 40 per cent. above the adult figure. This increase seems to be due chiefly to the process of growth which is lacking in the 36-year-old cretin. Although Benny's heat production is about half as great as that of a normal child of his size, we cannot consider him more than 20 per cent. below the normal for adults. The specific dynamic action of protein and carbohydrate, as we have said before, appears to be normal; but it is hard

TABLE 11.—Clinical—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Case 1 (Max W.)..	Prelim.	11:10	.....	.....	. ...	.....	.....	.....	.....
2/10/14									
61.76 Kg.	1	12:10	36.19	34.79	0.757	44.62	0.515	114.64	108.09
1.72 Sq. M.	2	1:10	39.28	37.60	0.760	46.04	0.515	124.08	116.54
								238.72	
Max W.	Prelim.	11:46	.....	.....	.....	.....	.....	.....	.....
2/18/14									
62.02 Kg.	1	12:46	41.81	33.14	0.917	42.53	0.658	113.45	111.71
1.72 Sq. M.	2	1:46	21.12	31.72	0.943	42.43	0.658	109.23	118.12
	3	2:46	38.26	33.13	0.840	42.25	0.658	111.22	114.40
								333.90	
Max W.	Prelim.	11:36	.....	.....	.....	.....	.....	.....	.....
2/20/14									
61.60 Kg.	1	12:36	32.77	31.90	0.747	40.14	0.466	104.85	102.72
1.73 Sq. M.	2	1:36	37.19	34.38	0.787	41.75	0.466	114.24	105.67
								219.09	
Max W.	Prelim.	10:45	.....	.....	.....	.....	.....	.....	.....
2/21/14									
62.26 Kg.	1	11:45	43.56	35.33	0.897	40.98	0.456	120.82	112.67
1.73 Sq. M.	2	12:45	45.07	33.52	0.978	41.85	0.456	117.20	116.41
								238.02	
Max W.	Prelim.	11:32	.....	.....	.....	.....	.....	.....	.....
2/25/14									
61.13 Kg.	1	12:32	41.19	36.32	0.825	39.35	0.817	121.27	114.35
1.71 Sq. M.	2	1:32	43.37	37.60	0.839	41.29	0.817	126.06	123.58
								247.33	
Max W.	Prelim.	11:18	.....	.....	.....	.....	.....	.....	.....
2/27/14									
60.86 Kg.	1	12:18	35.58	33.13	0.781	41.05	0.650	109.55	112.07
1.70 Sq. M.	2	1:18	35.94	34.25	0.763	41.90	0.650	112.78	112.12
								222.33	
Max W.	Prelim.	11:50	.....	....	.....	.. ..	.....	.....	.....
3 2/14									
60.47 Kg.	1	12:50	37.25	35.42	0.765	45.44	0.663	116.70	112.23
1.70 Sq. M.	2	1:50	38.75	32.28	0.873	46.48	0.663	109.25	112.08
								225.95	
Max W.	Prelim.	10:52	.....	.....	.....	.....	.....	.....	.....
3/4/14									
60.02 Kg.	1	11:52	31.79	30.79	0.751	39.10	0.550	101.10	105.05
1.70 Sq. M.	2	12:52	34.55	32.04	0.784	45.17	0.550	106.19	111.50
								207.29	
Max W.	Prelim.	11:06	.....	.....	.....	.....	.....	.....	.....
3 23/14									
59.20 Kg.	1	12:06	28.32	27.13	0.759	34.87	0.319	89.59	98.12
1.68 Sq. M.	2	1:06	29.31	27.63	0.771	34.44	0.319	91.46	97.22
	3	2:06	31.76	29.39	0.786	37.98	0.319	97.79	96.40
								278.84	

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
.....	37.41	...	....	.....	..	..	..	....	.....	Basal
103.52	37.33	131	31.4	0.750	12	75	13	1.85	59.58	Restless
125.28	37.51	142	14.6	0.754	11	75	14	2.01	64.49	Restless
228.80										
.....	37.04	...	....	.....	..	..	..	....	.....	Dextrose in lemonade, 100 gm. at 10:55-11:00
103.40	36.89	127	20.0	0.940	15	17	68	1.83	58.78	
110.83	36.87	123	20.8	0.972	16	8	76	1.76	56.60	
115.92	36.84	123	31.2	0.847	16	44	40	1.80	57.63	
330.15										
.....	36.96	...	....	.....	..	..	..	....	.....	Basal
87.44	36.67	108	16.0	0.739	12	78	10	1.70	54.58	Quiet
123.60	37.03	114	21.5	0.784	11	65	24	1.85	59.47	Quiet
211.04										
.....	36.76	...	....	.....	..	..	..	....	.....	Dextrose in lemonade, 100 gm. at 9:55 9:57
108.59	36.69	103	25.7	0.908	10	28	62	1.94	62.47	Quiet
117.48	36.72	107	60.0	0.997	10	1	89	1.88	60.60	Restless
226.07										
.....	37.44	...	....	.....	..	..	..	....	.....	Protein meal; N = 8.9 gm. at 10 a. m.
111.31	37.39	139	19.6	0.829	18	48	34	1.98	63.46	Quieter
129.64	37.52	137	33.0	0.846	17	44	39	2.06	65.97	Quieter
240.95										
.....	37.12	...	....	.....	..	..	..	....	.....	Basal
105.53	37.00	137	47.6	0.776	16	64	20	1.80	57.51	Restless
113.14	37.01	135	56.0	0.755	15	71	14	1.85	59.20	Restless
218.67										
.....	37.08	...	....	.....	..	..	..	....	.....	Protein meal; N = 9.0 gm. at 10:04 a. m.
112.64	37.10	98	35.6	0.757	15	70	15	1.93	61.52	Asleep 15 min.
119.50	37.26	103	41.2	0.887	16	32	52	1.81	57.59	Quiet
232.14										
.....	37.12	...	....	.....	..	..	..	....	.....	Basal
93.60	36.90	99	15.3	0.741	14	76	10	1.68	53.55	Asleep all the hour
110 52	36.89	116	58.0	0.781	14	64	22	1.77	56.24	Awake
204.12										
.....	36.94	...	....	.....	..	..	..	....	.....	Basal
92.25	36.83	88	15.2	0.754	9	76	15	1.51	47.91	Asleep 45 min.
95.27	36.80	87	24.1	0.768	9	72	19	1.55	48.91	Asleep 24 min.
101.70	36.92	85	25.4	0.784	9	67	24	1.65	52.29	Fairly quiet
289.22										

TABLE 11.—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Max W.	Prelim.	11:15	.....	.....	.....	.....	.....	.....	.....
4/6/14									
61.32 Kg.	1	12:15	30.11	27.75	0.789	30.36	0.402	92.23	91.14
1.71 Sq. M.	2	1:15	32.13	29.98	0.779	35.74	0.402	99.44	99.65
	3	2:15	33.39	30.43	0.798	40.02	0.402	101.44	102.02
								293.11	
Max W.	Prelim.	11:13	.....	.....	.....	.....	.....	.....	.....
4/24/14									
63.35 Kg.	1	12:13	33.83	31.77	0.774	34.51	0.554	105.02	97.07
1.75 Sq. M.	2	1:13	35.04	32.60	0.782	39.93	0.554	108.00	106.82
								213.02	
Max W.	Prelim.	11:12	.....	.....	.....	.....	.....	.....	.....
4/23 15									
73.27 Kg.	1	12:12	32.82	31.30	0.763	45.09	0.669	102.84	103.95
1.854 Sq. M.	2	1:12	35.71	33.68	0.771	51.97	0.669	110.98	113.02
								213.82	
Case 2 (Edw. T.)..	Prelim.	11:06	.....	.....	.....	.....	.....	.....	.....
3/3/15									
49.75 Kg.	1	12:06	29.78	.....	.....	40.78	0.506	.....	87.99
1.475 Sq. M.	2	1:06	30.48	28.26	0.785	43.55	0.506	93.59	94.69
	3	2:36	42.85	40.61	0.767	68.26	0.506	133.87	134.88
								227.46	
Edw. T.	Prelim.	11:00	.....	.....	.....	.....	.....	.....	.....
3/5/15									
50.39 Kg.	1	12:00	31.68	25.98	0.887	47.66	0.913	87.46	92.27
1.483 Sq. M.	2	1:00	33.04	27.48	0.874	46.16	0.913	92.31	96.99
	3	2:00	31.61	26.99	0.852	45.40	0.849	90.32	93.20
	4	3:00	29.97	26.74	0.815	45.94	0.849	88.62	95.06
								358.71	
Edw. T.	Prelim.	10.44	.....	.....	.....	.....	.....	.....	.....
3/6/15									
50.00 Kg.	1	11.44	27.56	23.99	0.836	36.38	0.583	80.18	84.34
1.478 Sq. M.	2	12:43	25.72	23.88	0.783	33.64	0.573	78.84	77.52
								159.02	
Edw. T.	Prelim.	11:02	.....	.....	.....	.....	.....	.....	.....
3/8/14									
49.69 Kg.	1	12:02	30.74	27.57	0.811	45.28	0.966	91.02	95.40
1.474 Sq. M.	2	1:02	32.81	29.73	0.803	43.97	1.006	98.11	98.78
	3	2:02	31.85	27.44	0.844	40.31	1.006	91.32	91.73
								280.45	
Edw. T.	Prelim.	10:56	.....	.....	.....	.....	.....	.....	.....
3 10/15									
49.32 Kg.	1	11:56	24.59	22.82	0.784	29.58	0.541	75.36	79.29
1.47 Sq. M.	2	12:56	29.05	26.22	0.806	32.30	0.541	87.29	88.84
								162.65	

—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
.....	36.68	...	....	.....	..	..	..	....	.....	Basal
86.09	36.59	93	25.4	0.787	12	64	24	1.51	48.16	Asleep 50 min.
108.27	36.67	90	55.0	0.776	11	68	21	1.62	51.93	Very restless
108.13	36.80	102	67.0	0.797	10	62	28	1.65	52.97	Very restless
297.47										
.....	36.68	...	....	.....	..	..	..	....	.....	Basal
100.23	36.75	125	40.5	0.769	14	68	18	1.66	53.66	
114.21	36.90	115	57.0	0.778	14	65	21	1.71	55.19	
214.44										
.....	37.04	...	....	.....	..	..	..	....	.....	Basal
93.62	36.87	101	21.0	0.753	17	70	13	1.40	47.70	Asleep 30 min.; quiet
111.22	36.85	97	33.0	0.764	16	69	15	1.52	51.48	Asleep 5 min.; quiet
204.84										
.....	37.72	...	....	.....	..	..	..	....	.....	Basal
85.15	37.66	99	35.0	.....	..	..	..	....	.....	Restless
88.14	37.51	98	23.0	0.781	14	64	22	1.88	56.21	Reading 45 min.
131.13	37.45	99	46.0	0.763	10	73	17	1.79	53.61	Asleep 50 min.
219.27										
.....	37.93	...	....	.....	..	..	..	....	.....	Protein meal*
77.14	37.58	90	6.0	0.922	28	20	52	1.74	52.06	Asleep 60 min.
80.52	37.20	87	14.0	0.902	26	25	49	1.83	54.95	Reading 52 min.
94.40	37.29	86	19.0	0.869	25	33	42	1.79	53.76	Quiet
93.40	37.32	88	15.0	0.819	25	46	29	1.76	52.75	Reading 30 min.; quiet 30 min.
345.46										
.....	37.25	...	....	.....	..	..	..	....	.....	Basal
81.35	37.19	85	6.0	0.844	19	44	37	1.60	47.93	Reading 60 min.; very quiet
84.89	37.38	88	18.0	0.778	19	60	21	1.58	47.11	Asleep 55 min.; fairly quiet
166.24										
.....	37.93	...	....	.....	..	..	..	....	.....	Meat; 10.19 gm. N at 8:55-9:04
88.69	37.78	93	19.0	0.814	28	46	26	1.83	54.70	Asleep 60 min.
85.37	37.47	95	5.0	0.802	26	50	24	1.97	58.96	Reading 60 min.
88.96	37.46	97	42.0	0.862	29	34	37	1.84	54.88	Awake, restless
263.02										
.....	37.87	...	....	.....	..	..	..	....	.....	Basal
69.79	37.65	89	16.0	0.789	16	60	24	1.53	45.51	Asleep, slightly restless
73.34	37.28	95	18.0	0.777	14	64	22	1.77	52.71	Reading 55 min.
143.13										

* Protein = 56.0 gm. (Nitro. = 8.95 gm.); Fat = 8.5 gm ; Carbh. = 47.1 gm.; 8:55 to 9:32 a. m.

TABLE 11.—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Edw. T.	Prelim.	11:07	.....	.....	.....	.....	.....	.....	.....
3/22/15									
49.17 Kg.	1	12:07	25.80	23.71	0.791	35.67	0.348	78.86	82.01
1.468 Sq. M.	2	1:07	29.12	26.38	0.803	35.17	0.348	88.01	87.01
	3	2:07	30.48	28.59	0.775	42.45	0.348	94.78	92.51
								261.65	
Edw. T.	Prelim.	11:33	.....	.....	.....	.....	.....	.....	.....
5/11/15									
50.37 Kg.	1	12:33	31.02	28.27	0.798	48.24	0.452	96.16	95.55
1.483 Sq. M.	2	1:33	33.75	34.47	0.712	59.87	0.452	115.11	107.61
								211.27	
Edw. T.	Prelim.	11:35	.....	.....	.....	.....	.....	.....	.....
11/1/15									
52.63 Kg.	1	12:35	31.77	29.39	0.786	53.39	0.358	97.73	95.07
1.508 Sq. M.	2	1:35	33.17	30.60	0.789	51.38	0.358	101.89	95.48
Case 3 (Jas. McE.)	Prelim.	11:16	.....	.....	.....	.....	.....	.....	.....
3/12/15									
41.16 Kg.	1	12:16	31.34	28.78	0.792	40.88	0.398	95.77	91.74
1.319 Sq. M.	2	1:16	30.92	29.96	0.751	45.31	0.398	98.57	96.66
	3	1:46	16.67	15.27	0.794	22.09	0.398	50.84	48.20
								245.18	
James McE.	Prelim.	11:00	.....	.....	.....	.....	.....	.....	.....
3/31/15									
39.98 Kg	1	12:00	30.55	26.24	0.846	29.79	0.316	88.61	80.65
1.303 Sq. M.	2	1:00	31.49	28.62	0.800	33.38	0.316	95.60	86.04
								184.21	
James McE.	Prelim.	11:12	.....	.....	.....	.....	.....	.....	.....
5/14/15									
45.29 Kg.	1	12:12	32.14	31.91	0.732	55.70	0.301	104.91	96.97
1.371 Sq. M.	2	1:12	33.34	31.25	0.776	58.92	0.301	103.73	101.66
								208.64	
Case 4 (Dr.G.S.L.)	Prelim.	11:08	.....	.....	.....	.....	.....	.....	.....
4 9 14									
71.78 Kg.	1	12:08	33.19	31.92	0.756	30.25	0.393	105.33	105.66
1.89 Sq. M.	2	1:08	33.30	30.88	0.784	30.23	0.393	102.62	102.22
								207.95	
Dr. G. S. L.	Prelim.	11:20	.....	.....	.....	.....	.....	.....	.....
4/16/14									
69.40 Kg.	1	12:20	32.58	31.94	0.742	35.50	0.460	104.83	106.58
1.86 Sq. M.	2	1:20	34.95	33.05	0.769	38.16	0.460	109.29	102.25
								214.12	
Case 5 (Peter N.)..	Prelim.	11:23	.....	.....	.....	.....	.....	.....	.....
4/14/15									
63.44 Kg.	1	12:23	22.85	20.32	0.818	28.42	0.375	67.89	77.85
1.795 Sq. M.	2	1:23	24.71	21.14	0.850	28.19	0.375	71.28	76.70
								139.17	

—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
.....	37.11	...	....	.....	..	..	..	....	.....	Basal
76.63	36.99	100	....	0.790	12	63	25	1.60	47.71	Sleeping, very quiet
80.53	36.83	108	10.0	0.803	10	61	29	1.79	54.48	Reading, quiet
97.31	36.97	112	30.0	0.772	10	70	20	1.72	57.34	Sleeping
254.47										
.....	37.23	...	....	.....	..	..	..	....	.....	Basal after ligation
95.83	37.25	131	15.0	0.772	12	69	19	1.91	57.31	Restless
106.76	37.24	137	34.0	0.683	10	90	0	2.29	68.60	Restless
202.59										
.....	37.16	...	....	.....	..	..	..	....	.....	Basal 6 mos. after ligation
90.04	37.06	96	18.0	0.786	10	66	24	1.86	56.5	Quiet; sleeping
100.06	37.18	107	14.0	0.789	9	67	26	1.94	58.9	Quiet; awake
.....	38.26	...	....	.....	..	..	..	....	.....	Basal
87.48	38.15	105	14.0	0.790	11	64	25	2.33	65.24	Quiet; reading
92.07	38.03	110	23.0	0.744	11	79	10	2.40	67.15	Quiet; reading
51.66	38.21	114	15.0	0.793	10	64	26	2.47	69.26	Fairly quiet
231.21										
.....	36.83	...	....	.....	..	..	..	....	.....	Basal after quinin and ergotin
82.62	36.80	95	10.0	0.851	9	46	45	2.22	61.54	Quiet; reading
94.47	37.21	99	26.0	0.800	9	62	29	2.39	66.39	Reading 32 m.n.; restless 28 m.n.
177.09										
.....	37.20	...	....	.....	..	..	..	....	.....	Basal after ligation
89.64	37.02	111	14.0	0.726	8	85	7	2.32	68.61	Fairly quiet
101.86	37.04	119	7.0	0.773	8	72	20	2.29	67.81	Fairly quiet
191.50										
.....	36.57	...	..	.....	..	..	..	....	.....	Basal
104.54	36.56	98	24	0.751	10	76	14	1.47	49.54	Quiet
102.91	36.58	101	16	0.782	10	67	23	1.43	48.27	Quiet
207.45										
.....	36.88	...	..	.....	..	..	..	....	.....	Basal; at 9:37 9:50 a. m. 1.0 c.c. thyroid "residue"
101.60	36.80	97	29	0.733						
104.17	36.84	101	58	.0764	12	80	8	1.51	50.42	Fairly quiet
205.77					11	71	18	1.57	52.57	Restless
.....	37.27	...	..	.....						
73.79	37.15	71	6	0.820	..	..	..	....	.....	Basal
75.80	37.13	71	2	0.858	15	52	33	1.07	34.66	Very quiet
149.59					14	41	45	1.12	36.39	Very quiet

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Case 6 (Anna K.)..	Prelim.	11:12	.....	.....	.....	.....	.....	.....	.....
4 28/14									
44.45 Kg.	1	12:12	31.73	31.25	0.738	49.35	0.407	102.57	97.70
	2	1:12	32.00	30.79	0.756	53.67	0.407	101.53	100.83
								204.10	
Anna K.	Prelim.	11:40	.....	.....	.....	.....	.....	.....	.....
5/13/14									
44.50 Kg.	1	12:40	27.62	24.63	0.816	33.43	0.505	82.14	69.53
	2	1:40	28.40	26.01	0.794	41.06	0.505	86.31	81.27
								168.45	
Case 7 (Anna R.)..	Prelim.	9:45	.....	.....	.....	.....	.....	.....	.....
5/10/13									
46.71 Kg.	1	10:45	22.05	21.02	0.763	29.44	0.287	69.42	61.67
	2	11:45	21.67	17.95	0.878	29.64	0.287	60.98	60.15
	3	12:45	22.55	22.15	0.740	35.40	0.287	72.74	65.27
								203.14	
Anna R.	Prelim.	9:30	.....	.....	.....	.....	.....	.....	.....
5/20 13									
42.91 Kg.	1	10:30	23.74	21.93	0.787	36.63	0.380	72.73	65.80
	2	11:30	24.72	23.55	0.763	43.42	0.380	77.68	72.33
	3	12:30	24.16	24.52	0.717	49.82	0.380	80.01	83.34
								230.41	
Anna R.	Prelim.	9:38	.....	.....	.....	.....	.....	.....	.....
5 28/13									
43.29 Kg.	1	10:38	23.15	22.21	0.758	42.19	0.423	73.04	71.31
	2	11:38	22.13	21.01	0.766	38.89	0.423	69.19	67.88
	3	12:38	23.19	21.29	0.792	44.42	0.423	70.60	74.19
								212.83	
Anna R.	Prelim.	11:13	.....	.....	.....	.....	.....	.....	.....
5/14/14									
48.20 Kg.	1	12:13	22.79	20.90	0.793	29.00	0.282	69.58	59.76
	2	1:13	23.55	21.86	0.784	30.09	0.282	72.63	65.43
								142.21	
Case 8 (Sarah M.)	Prelim.	11:20	.....	.....	.....	.....	.....	.....	.....
4 29 14									
55.96 Kg	1	12:20	25.62	23.85	0.781	37.86	0.363	79.07	76.95
	2	1:20	25.28	23.79	0.773	37.09	0.363	78.70	79.67
								157.77	
Case 9 (Marion B.)	Prelim	11:35	.....	.....	.....	....	.....	.....	.....
2/5/15									
57.91 Kg.	1	12:35	25.89	25.26	0.746	35.16	0.195	83.30	80.18
	2	1:35	25.80	23.59	0.796	35.15	0.195	78.91	79.99
	3	2:35	26.10	24.44	0.775	37.01	0.195	81.35	86.23
								243.56	
Case 10 (Mrs. L.)..	Prelim.	11:18	.....	.....	.....	.....	.....	.....	.....
4 20/14									
63.00 Kg.	1	12:18	25.45	25.30	0.732	40.91	0.382	82.79	85.12
	2	1:18	26.64	24.35	0.795	40.10	0.382	81.00	84.18
								163.79	

—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
.....	37.18	...	..	.....						
95.12	37.12	118	36	0.730	..	..	..	....	.....	Basal
98.98	37.08	123	38	0.750	11	82	7	2.31	66.39	Restless
194.10					11	76	13	2.28	65.71	Quiet
.....	37.04	...	..	.....						
71.74	37.11	95	10	0.818	..	..	..	....	.....	Basal
83.84	37.19	105	13	0.792	16	52	32	1.85	54.37	Very quiet
155.58					16	59	25	1.94	55.83	Very quiet
.....	37.39	119	..	.....						
59.36	37.34	...	30	0.758	..	..	..	....	.....	Basal
61.31	37.38	...	14	0.890	11	73	16	1.49	44.50	
65.65	37.40	...	36	0.783	12	33	55	1.31	39.09	
186.32					10	82	8	1.56	46.63	
.....	37.87	...	..	.....						
65.02	37.99	...	3	0.784	..	..	..	....	.....	Basal
67.81	37.98	...	12	0.757	14	63	23	1.69	48.23	Quiet
81.02	38.04	...	11	0.703	13	72	15	1.81	51.51	Quiet
213.85					13	87	0	1.86	53.06	Quiet
.....	37.16	...	..	.....						
66.87	37.16	...	..	0.749	..	..	..	....	.....	Basal
65.89	37.23	...	..	0.758	15	73	12	1.69	49.99	
69.74	37.23	...	..	0.789	16	69	15	1.60	47.36	
202.50					16	60	24	1.63	48.32	
.....	36.69	...	..	.....	..	..	..	....	.....	Basal 1 yr. later
67.01	36.88	97	9	0.791	11	63	26	1.44	42.69	Very quiet; dozed
69.07	36.98	97	10	0.781	10	67	23	1.51	44.56	Very quiet; dozed
136.08										
.....	37.33	...	..	.....	..	..	..	....	.....	Breakfast at 7 a. m.: toast 20 gm., milk 250 c.c.
73.30	37.26	97	24	0.778	12	66	22	1.41	43.90	Fairly quiet
77.44	37.22	86	33	0.768	12	69	19	1.40	43.70	Fairly quiet
150.74										
.....	37.00	...	..	.....	..	..	..	....	.....	Basal
73.61	36.87	114	46	0.742	6	83	11	1.44	45.20	Restless
82.04	36.92	132	31	0.795	7	63	30	1.36	42.82	Restless
84.82	36.91	136	36	0.773	6	73	21	1.41	44.14	Reading
240.47										
.....	38.18	...	..	.....	..	..	..	....	.....	Basal
81.05	38.11	81	26	0.721	12	84	4	1.31	42.46	Restless
80.67	38.05	88	36	0.794	12	62	26	1.29	41.54	Restless
161.72										

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Case 11 (Bessie H.)	Prelim.	11:40	.....	.....	.....	.....	.....	.....	.....
4/8/14	1	12:40	19.06	17.02	0.815	26.67	0.159	57.12	62.51
47.06 Kg.	2	1:40	19.41	16.68	0.846	26.21	0.159	56.44	61.34
1.42 Sq. M.								113.56	
Bessie H.	Prelim.	11:27	.....	.....	.....	.....	.....	.....	.....
4/13/14	1	12:27	18.42	16.22	0.826	20.31	0.125	54.63	56.23
48.18 Kg.	2	1:27	19.49	17.83	0.795	21.81	0.125	59.60	59.33
1.43 Sq. M.								114.23	
Bessie H.	Prelim.	11:05	.....	.....	.....	.....	.....	.....	.....
4/18/14	1	12:05	17.83	15.14	0.856	22.12	0.217	51.02	52.61
46.62 Kg.	2	1:05	18.57	16.57	0.815	23.29	0.217	55.49	54.87
1.41 Sq. M.								106.51	
Case 12 (Benny L.)	Prelim.	11:40	.....	.....	.....	.....	.....	.....	.....
4/10/14	1	12:40	10.28	7.67	0.974	10.45	0.363	26.10	31.38
22.80 Kg.	2	1:40	10.23	8.58	0.867	10.51	0.363	28.63	32.70
0.829 Sq. M.								54.73	
Benny L.	Prelim.	11.52	.....	.....	.....	.....	.....	.....	.....
4/14/14	1	12:52	13.13	9.40	1.016	12.54	0.293	32.58	32.32
23.60 Kg.	2	1:52	12.81	9.24	1.008	12.29	0.293	31.97	33.39
0.84 Sq. M.	3	2:52	12.05	8.99	0.975	11.69	0.293	30.91	33.82
								95.46	
Benny L.	Prelim.	11:10	.....	.....	.....	.....	.....	.....	.....
4/21/14	1	12:10	11.23	8.10	1.008	13.82	0.316	27.91	33.30
24.04 Kg.	2	1:10	11.02	8.90	0.899	13.47	0.316	30.13	32.12
0.847 Sq. M.	3	2:10	11.07	9.04	0.890	13.21	0.316	30.48	33.95
	4	3:10	11.15	8.79	0.923	12.94	0.316	29.86	33.30
								118.38	
Benny L.	Prelim.	11:10	.....	.....	.....	.....	.....	.....	.....
4/23/14	1	12:10	9.44	7.76	0.885	10.58	0.226	26.21	26.47
23.97 Kg.	2	1:10	9.20	7.83	0.855	11.21	0.226	26.25	28.57
0.847 Sq. M.								52.46	
Benny L.	Prelim.	11:20	.....	.....	.....	.....	.....	.....	.....
4/27/14	1	12:20	10.47	7.94	0.959	14.30	0.208	27.36	27.15
23.86 Kg.	2	1:20	10.75	8.33	0.939	13.79	0.208	28.58	29.55
0.847 Sq. M.	3	2:20	11.01	8.38	0.955	13.29	0.208	28.88	29.25
								84.82	
Benny L.	Prelim.	11:10	.....	.....	.....	.....	.....	.....	.....
5/1/14	1	12:10	10.86	10.05	0.785	11.67	0.236	33.22	31.09
23.03 Kg.	2	1:12	10.91	9.96	0.797	11.88	0.236	32.99	31.80
0.833 Sq. M.								66.21	

—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh.)	
.....	37.22	...	..	.....	..	.	..	. ..	. ...	Basal
75.89	37.06	60	4	0.815	7	29	64	1.22	35.59	Quiet
62.93	37.11	59	3	0.850	7	47	46	1.20	35.17	Quiet
118.82										
.... .	37.15	...	..	.....	..	..	..	....	. . .	Basal
51.06	37.03	72	8	0.828	6	55	39	1.13	33.52	Very quiet
62.55	37.12	75	13	0.795	6	66	28	1.24	36.56	Very quiet
113.61										
.....	37.19	...	..	.....	..	..	..	....	. . .	Basal; [illegible] food "residue" at 9:30 a. m.
51.86	37.18	98	8	0.847	11	46	43	1.10	31.99	Very quiet
52.18	37.12	90	15	0.816	10	56	34	1.19	.4 7	Very quiet
104.04										
.....	37.51	...	..	.....	..	..	..	....	.....	Basal
28.47	37.37	83	2	1.089	37	0	63	1.15	26.36	Very quiet
30.74	37.28	85	2	0.903	34	12	44	1.26	28.92	Very quiet
59.21										
.....	37.59	..	..	.....	..	.	.	....	.....	Lactose 100 gm.; water and lemon juice, 200 c.c.
30.10	37.49	89	2	1.092	24	0	76	1.38	32.16	Very quiet
32.56	37.46	89	2	1.083	24	0	76	1.35	31.56	Very quiet
31.62	37.36	87	2	1.040	25	0	75	1.31	30.51	Very quiet
94.28										
.....	37.41	..	..	.....	..	..	..	. ..	.....	Protein meal at 9:38-9:55 a. m.; N = 3.6 gm.
31.46	37.33	87	6	1.109	30	0	70	1.16	27.20	Very quiet
31.07	37.20	81	5	0.939	28	15	57	1.25	29.37	Very quiet
32.50	37.23	81	9	0.927	27	18	55	1.27	29.71	Quiet
31.46	37.15	78	10	0.974	28	6	66	1.24	29.10	Quiet
126.49										
.....	37.16	..	..	.....	..	..	..	....	.....	Basal
25.44	37.12	79	5	0.911	23	23	54	1.09	25.60	Very quiet
26.93	37.05	77	9	0.871	23	34	43	1.09	25.63	Quiet
52.37										
.....	37.34	..	..	.....	..	..	.	....	.....	Dextrose, 70 gm. at 10:20 - 10:32 a. m.
26.52	37.32	78	3	1.004	20	0	80	1.15	26.82	Very quiet
28.92	37.30	79	4	0.975	19	7	74	1.20	28.02	Very quiet
29.41	37.32	80	5	0.996	19	1	80	1.21	28.31	Very quiet
84.85										
. ....	37.76	..	..	.....	.	..	.	....	.....	Thyroid extract
30.07	37.72	94	3	0.781	19	60	21	1.44	33.33	Very quiet
31.92	37.74	95	4	0.795	19	56	25	1.43	33.10	Very quiet
61.99										

to find the proper basis on which to compare it with results obtained on normal adults. The administration of thyroid extract raised the metabolism to normal in three and a half days, increased the pulse rate from about 80 to 95, and made the patient sick and miserable.

THERAPEUTIC APPLICATIONS

Mental and physical rest is the surest means of securing the drop in the metabolism which indicates a diminution in the pernicious activity of the thyroid. Psychotherapy is of some value, and this combined with rest may account entirely for the improvement following most of the so-called medical cures. Previous observers have found little or no reduction in the oxidative processes after treatment with "Radogen," the serum of thyroidectomized horses, and the Roentgen ray. To this list may be added from the present work thyroid "residue," the ergotin and quinin hydrobromate treatment, and Beebe's serum. These remedies, however, were tried on but one or two patients, and a more favorable report might have been justified if more cases had been tested. In the treatment of hyperthyroidism, calorimeters and other forms of respiratory apparatus seem to be therapeutic nihilists.

Some observers have found a prompt drop in the metabolism after a partial thyroidectomy. Ligation of the arteries usually causes a distinct rise in heat production which may last several weeks. This shows that following a ligation of the arteries the patients should be kept as quiet as possible and thyroid extract should on no account be given.

It is quite possible that the above mentioned therapeutic agents control some of the minor symptoms of the disease or render the major symptoms less apparent to the patient and his physician. We cannot consider the patient to be anywhere near a cure until the metabolism has approached the normal. We cannot consider a therapeutic agent to be curative unless it causes the metabolism to approach the normal more quickly than the tendency toward spontaneous improvement aided by mental and physical rest.

The need of large amounts of food by exophthalmic goiter patients is clearly shown. There is no indication against the use of fairly liberal amounts of protein, and there is no reason to prefer the proteins of vegetables and milk to those of meat. The number of calories required per day varies with the weight of the patient, the severity of the case and the degree of muscular activity. In general, it may be said that exophthalmic goiter patients need from one and one-half times to twice as much food as a normal person under similar conditions. Several of the patients studied produced over 100 calories an hour while at rest. Max W. (Case 1) and Edwin T. (Case 2) showed a slightly negative nitrogen balance when receiving 3,500 and

4,000 calories a day. Every effort should be made to give food of high caloric value in large amounts, or there will be losses of body fat and protein.

SUMMARY AND CONCLUSIONS

The metabolism in exopthalmic goiter has been studied for the first time in a respiration apparatus which is also a calorimeter. Thirty-seven observations were made on eleven patients with this disease, and six experiments were made on a cretin. With some of the patients the nitrogen balance was also studied.

The measurement of the heat production gives us the best index of the severity of the disease and of the effect of treatment. Very severe cases show an increase of 75 per cent. or more above the normal average, severe cases 50 per cent. or more, and moderately severe and mild cases less than 50 per cent., while a few mild and several atypical or cases in which operation has been performed may be within normal limits. In severe cases the warmth of skin and sweating can be accounted for entirely by the necessity for the increased elimination of heat. At least a part of the tachycardia is due to the increased metabolism, and perhaps it might be possible to reproduce the extreme tachycardia, the cardiac enlargement, emaciation and mental irritability if we were able to stimulate the metabolism of normal men for twenty-four hours a day over a period of months or years.

The specific dynamic action of protein and of glucose is within normal limits, and there is no consistent difference between the effects of protein in meat and an equal amount in milk and eggs. One patient was able to derive 89 per cent. of his calories from carbohydrate in an experiment when he was showing an alimentary glycosuria. There is evidently no interference with the oxidation of carbohydrates.

The methods of direct and indirect calorimetry agree very closely when one considers the technical difficulties. The method of direct calorimetry gave results which were slightly lower than the indirect, the total difference being 2.9 per cent., and the average difference in the individual experiments being $\pm$ 4.1 per cent. This and the absence of abnormal respiratory quotients shows that the law of the conservation of energy holds good in exophthalmic goiter, and that there is no profound disturbance of the intermediary metabolism.

The average water elimination through skin and lungs in the severe and moderately severe cases of hyperthyroidism is 39.9 gm. per hour. The increase above the normal is closely proportional to the increase in heat production; 25.7 per cent. of the calories are dissipated through vaporization in goiter patients, whereas the mean normal is almost the same, 23.9 per cent.

The level of the heat production was used as an index of the effect of medical treatment. Rest in bed for a week or more caused a drop of more than 10 per cent. The effects of treatment with Beebe's serum, thyroid "residue" ergotin and quinin hydrobromate was less marked each being tested on one patient. Ligation of the thyroid arteries with three out of the four patients studied caused a distinct rise in metabolism, the duration of which was uncertain. There is as yet no proof that any conservative form of treatment causes a greater reduction of metabolism than mental and physical rest.

One small cretin 36 years old produced about half the calories eliminated by children of his size. As estimated by the surface area, his metabolism was about 20 per cent. below the normal adult level. Three and a half days of treatment with thyroid extract raised his heat production to normal.

NOTE.—The work here reported was made possible by the cooperation of a number of associates who should receive credit for the major part of the work. The analyses of food, urine and feces were made by Mr. Frank C. Gephart, with the assistance of Mr. R. H. Harries and Mr. R. C. Stone. The electrical control of the calorimeter was in charge of Mr. G. F. Soderstrom, and the residual air analyses and calculations were made by Dr. A. L. Meyer and Mr. Harries. The results were checked and tabulated by Miss Grace Sims and Mr. Stone. Miss Estelle Magill and her assistants, Miss A. Honold, Miss M. M. Fauquier and others were responsible for the weighing and preparation of the food, the care of the patients and the collection of specimens.

I wish to express my thanks to Dr. John Rogers for providing most of the patients and for cooperating very actively in the work. I also wish to thank Dr. S. P. Beebe for supervising the serum treatment and Dr. G. R. Lockwood of the First Medical Division of Bellevue for permitting the use of material from his ward, and to Drs. W. H. Brundage, T. C. Janeway and R. J. Shea, who also sent patients for treatment and observation.

CLINICAL CALORIMETRY

FIFTEENTH PAPER

THE BASAL METABOLISM IN PERNICIOUS ANEMIA*

A. L. MEYER, M.D., AND EUGENE F. DU BOIS, M.D.
NEW YORK

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      Comparison with average normal metabolism.
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HISTORICAL

The view that a paucity of hemoglobin must seriously impair the oxidative processes of the body received dogmatic credence for many years. Although based on *a priori* considerations, it was apparently supported by animal experimentation, chiefly that of Bauer.[1] In Bauer's experiments the effect of hemorrhage is difficult of ascertainment. Food, fasting and the mechanical effect of blood loss are disturbing factors. The vomiting of Bauer's dog leads one to suspect that the animal was unfit for the purpose in hand.

At any rate, subsequent investigation on animals failed to substantiate any pronounced fall in the metabolic functions of the body in anemia. The observations of Finkler,[2] Lukjanow,[3] Pembrey[4] and

* Submitted for publication Feb. 4, 1916.

* From the Russell Sage Institute of Pathology, in Affiliation with the Second Medical Division, Bellevue Hospital.

1. Baur: Ueber die Zersetzungsvorgänge im Thierkörper unter dem Einfluss von Blutenziehungen, Ztschr. f. Biol., 1872, viii, 567.

2. Finkler Ueber den Einfluss der Strömungsgechwindichkeit und Menge des Blutes auf die tierische Verbrennung. Arch. f. d. ges. Physiol. (Pflüger's), 1875, x, 368.

3. Lukjanow: Ueber die Aufnahme von Sauerstoff bei Erhöhthem Procentegehalt desselben in der Luft, Ztschr. f. Phys. Chem., 1883, viii, 315.

4. Pembrey: Influence of Bleeding and Transfusion on Respiratory Exchange, Jour. Physiol., 1895, xv, 449.

Gürber and Delchef[5] effected a modification of the current hypothesis, inasmuch as no permanent departure from the normal metabolism could be found. There are variations, to be sure, but the tendency is distinctly toward normality. The slight increase in heat production which Fredericq[6] measured with the d'Arsonval compensation calorimeter is well within the limits of the experimental error. Only once did Hari,[7] working in Tangl's laboratory with a Rubner calorimeter, find an increase of 12 per cent. in the heat production of a dog.

The anemias in animals have been artificially induced by bloodletting. It is open to question whether the anemias studied in animals are at all comparable with those obtaining in the clinic. When we come to the application of experimental methods to clinical anemia, the problem at once becomes decidedly more complicated. In addition to the simple anemias, there is the unique type of pernicious anemia. Chlorosis and leukemia may be included in the category because of their low hemoglobin content. Any difference that the clinical forms show may, quite apart from refinement of technic, be ascribed to essential differences between anemias artificially induced and anemias arising from pathologic agencies.

Magnus-Levy[8] points out that Pettenkofer and Voit's pioneer experiment on a leukemic man, if properly interpreted, actually reveals an increase in the metabolism.

Both Kraus[9] and Bohland[10] find the metabolism near the upper physiologic limits, and that in some cases (Bohland) it may really exceed these limits. Thiele and Nehring,[11] while observing a slight increase in secondary anemia, could not establish a diminution in the oxygen intake in chlorotics. In the hands of Magnus-Levy,[12] pernicious anemia yields a metabolism somewhat elevated. Grafe[13] finds

5. Gürber and Delchef: Einfluss des Aderlasses und der Transfusion auf den Wert des Atmungsstoffwechsel, Jahresb. ü. d. Fortschr. d. Thierchem. (Maly's), 1906, p. 561.

6. Fredericq: De l'action physiologique des soustractions sanguines, Jahresb. ü. d. Fortschr. d. Thierchem. (Maly's), 1887, p. 377.

7. Hari: Der Einfluss grosser Blutverluste auf die Kohlensäure—und Wasserausscheidung und Wärmeproduction, Arch. f. d. ges. Physiol. (Pflüger's), 1909, pp. 130, 187.

8. Magnus-Levy: Ueber den Stoffwechsel bei einem leukämischen Mannes, Ztschr. f. Biol., 1869, v, 319.

9. Kraus: Ueber den Einfluss von Krankheiten auf den respiratorischen Gaswechsel, Ztschr. f. klin. Med., 1893, xxii, 458.

10. Bohland: Ueber den respiratorischen Gaswechsel bei verschiedenen Formen der Anämie, Berl. klin. Wchnschr., 1893, xviii, 417.

11. Thiele and Nehring: Gaswechsel bei anämischen zuständen, Ztschr. f. klin. Med., 1896, xxx, 41.

12. Magnus-Levy: Der Einfluss von Krankheiten auf den Energiesaushalt im Ruhestand, Ztschr. f. klin. Med., 1906, lx, 179.

13. Grafe: Die Steigerung des Stoffwechsels bei chronischer Leukämie, Arch. f. klin. Med., 1911, cii, 406.

an amazing augmentation in leukemia. The results of these observers will receive further consideration.

EXPERIMENTAL PROCEDURE

The six cases of anemia which we wish to present were all studied from sixteen to eighteen hours after the last meal. The patients were at rest and in the lying posture. They were allowed to turn in bed occasionally and move their arms a little. While it is desirable that there should be no unnecessary movements, we believe the subject should be as comfortable as the conditions of the experiment will permit.

The exact routine previous to the actual observation has received detailed consideration in another place.[14] The body temperature was measured by means of an electric resistance thermometer placed in the rectum. Surface thermometers were not used. It has been found that when there are no rapid fluctuations in body temperature the rectal temperature is the more reliable but is by no means absolutely satisfactory. Owing to the limitations of the rectal thermometer, and its failure to register accurately the mean temperature changes of the body, we still use the method of indirect calorimetry as a standard, for reasons previously discussed.

HISTORIES OF PATIENTS

Case 1.—*History.*—Daniel V. (splenic anemia, congenital syphilis), aged 21 years, elevator boy, white, French West Indies, admitted April 16, 1913, discharged July 30, 1913, had severe dysentery in 1897, and tropical fever with black stools in 1902. He had pain in the left side in 1910. He came to New York in 1912. A fine rash appeared on the body, March 30, 1913, and the patient became pale. March 27 and again two weeks later, he vomited blood.

Physical Examination.—April 16, the patient was tall and thin, with porcelain colored skin. Soft systolic murmur. Spleen palpable 7 cm. below costal margin. Hemoglobin, 25 per cent.; erythrocytes, 1,700,000. Differential count normal except for 1.5 per cent. myelocytes. Wassermann reaction positive. April 19, transfusion, 500 c.c. Spleen larger. April 23, transfusion, 750 c.c. April 24, spleen 11 cm. below costal margin in midclavicular line. Dark stools. April 26, transfusion, 760 c.c. Hemoglobin, 25 per cent.; erythrocytes, 1,976,000. May 9, patient put in the calorimeter. Blood pressure: systolic, 108; diastolic, 48; temperature 99-100; pulse 96; respiration 20; stools, four or five every day. Wassermann positive.

The spleen was removed several weeks later, and the patient improved rapidly. He was seen a year later in good health.

Case 2.—*History.*—Andrew K.[15] (pernicious anemia), aged 27, plumber, entered the hospital Sept. 10, 1911, with a high grade of anemia. He improved

14. Gephart, F. C., and Du Bois, E. F.: Clinical Calorimetry, Fourth Paper, The Determination of the Basal Metabolism of Normal Men and the Effect of Food, The Archives Int. Med., 1915, xv, 835.

15. Case reported by Coleman and Hartwell: Med. Rec., New York, 1914, lxxxv, 1160.

under the syrup of ferrous iodid, sodium cacodylate and Blaud's pills. He was discharged Nov. 1, 1911, and readmitted June 23, 1913. He worked as street car conductor but had to stop work because of weakness. There was no history of syphilis.

Physical Examination.—The patient's skin was lemon yellow, there was extensive pigmentation, and the teeth were in bad condition. The spleen was three fingers' breadth below the costal margin. Jan. 24, 1913, the hemoglobin was 50 per cent.; erythrocytes, 1,600,000; marked anisocytosis and poikilocytosis. Slight polychromatophylia. Leukocytes, 6,000. Stools negative. During the ensuing four months there were low, continued fever, attacks of diarrhea, progressive weakness and high pulse rate. Several transfusions were made. The last transfusion was interrupted by hemolysis. Two hours later severe chills and temperature of 103.8. Four hours later, 2 ounces of bloody urine.

Treatment and Course.—July 8, normoblasts 26 to every 100 leukocytes. Leukocytes, 2,000; polymorphonuclears, 64 per cent.; lymphocytes, 30 per cent.; large mononuclears, 3 per cent. October 29, splenectomy. Cytologic details essentially those of erythrogenesis and myelogenesis. November 3, lemon yellow color disappeared. Picture of severe secondary anemia. November 17, leukocytes 12,000. December 6, leukocytes 16,000. December 29, hemoglobin, 27 per cent.; erythocytes, 1,280,000; normoblasts, 51, and megaloblasts 11 to every 200 leukocytes. Jan. 6, 1914, leukocytes, 22,400; January 13-29, neosalvarsan. Patient grew weaker. February 25, hemoglobin, 18 per cent.; erythrocytes, 1,264,000. Normoblasts 111 and megaloblasts 16 to every 200 leukocytes. March 11 and 17, patient put in calorimeter. Pulse during March ranged from 100 to 124; respirations from 24 to 28; blood pressures: systolic, 142; diastolic, 50 (March 27); temperature, from 99 to 100. April 24, patient looked and felt better. Beginning to sit up. April 28, Wassermann reaction positive. Patient died December, 1915.

Case 3.—*History.*—Martin C. (pernicious anemia, transverse myelitis), driver, aged 32, admitted Jan. 8, 1915, died December, 1915, complained chiefly of weakness, shortness of breath, palpitation and paralysis of legs. In 1905 he slipped and had a bad fall which left him with a persistent pain between the shoulders. One year later the pains suddenly disappeared, but his legs began to grow numb and he lost good control of his feet. Soon after he was unable to walk and unable to control his bowels. In 1912 he began to grow stronger, and was able to walk with crutches. In February, 1914, he noticed general weakness. In December, a month before admission, he began to suffer from anemia, dyspnea, palpitation, nausea and insomnia.

Physical Examination.—January 8, the patient was very pale, poorly developed and poorly nourished. Cardiac impulse forceful and diffuse. Apex in fifth space 5.6 cm.; left border 12 cm. from midsternal line; base in third space. Presystolic thrill over precordium. Presystolic murmur and systolic murmur at apex, the latter transmitted to axilla. Systolic murmur at aortic area. Corrigan pulse. Spleen palpable. Legs paralyzed, wasted and atrophic. Babinski reflex present. Lymph nodes generally enlarged. Incontinent of urine. January 13, eyegrounds showed presence of old retinal hemorrhages. January 20, erythrocytes, 650,000; normoblasts, 47; megaloblasts, 6. Anisocytosis, poikilocytosis and polychromatophylia marked. January 29, patient in the calorimeter. January 28 to February 23, temperature from 99 to 101; pulse from 100 to 124; respirations, from 20 to 30. February 2, hemoglobin 23.4 per cent. February 10, fluid on left side of chest. Thoracentesis. February 16, hemoglobin, 20 per cent. February 27, dulness on left side persisted. March 17, heart not enlarged. Systolic murmur over second left space and over apex. Edge of liver felt indistinctly at umbilicus. March 23, erythrocytes, 472,000; leukocytes, 2,600; anisocytosis and poikilocytosis very marked. May 4, patient put in calorimeter. Hemoglobin, 21 per cent. Apex impulse diffuse. Left limit dul-

ness, fifth space, 13 cm.; fourth space, 11.8 cm.; third space, 10 cm.; right limit, 2.8 cm. from midsternal line. Loud booming systolic murmur at apex. To left of sternum there was a soft blowing sound in diastole. Posteriorly left side flatness below angle of scapula. Patient later got up in a chair and dressed himself. Slightly jaundiced. April 24 to May 22, temperature normal to 100; pulse 72 to 115; respiration, 20 to 24. At necropsy in December, 1915, a bony tumor was found pressing on the spinal cord, causing a transverse myelitis.

Case 4.—*History.*—Bartolo D. (pernicious anemia), aged 50, laborer, admitted Feb. 22, 1915, discharged March 21, 1915, complained chiefly of weakness, and pain in abdomen. Four months ago he felt sick but was able to continue work.

Physical Examination.—February 22, poorly nourished. Appearance chronically ill. Skin of peculiar greenish yellow. Conjunctiva pale. Heart regular in rate, force and rhythm. Soft systolic murmur over entire precordium. Pulse regular in rate, force and rhythm. Tension low. Vessel walls thickened. Slight distention of abdomen. Extremities wasted. General lymphatic enlargement. February 23, blood pressure 95 (systolic). February 24, temperature rose to 100.7, after which it remained below 100. Pulse varied from 80 to 100. February 28, blood pressure, systolic, 92; diastolic, 70. March 4, stools negative. March 5, red cells 1,328,000; hemoglobin, 27 per cent.; megaloblasts, 6; leukocytes, 4,200; polymorphonuclears, 71; lymphocytes, 28. March 15, condition unchanged. Patient put in calorimeter. Complained of weakness and toothache. Stools large, possibly due to poor absorption. On strong positive nitrogen balance. March 18, red cells, 2,200,000; hemoglobin, 44 per cent. Wassermann reaction negative.

Case 5.—*History.*—Daniel O. (pernicious anemia, mitral stenosis and insufficiency), aged 38, steam fitter, admitted April 11, 1915, discharged May 10, 1915, complained chiefly of dizziness and weakness. Pain in lower lumbar region. The patient was moderately alcoholic. In 1905, kidney trouble. Had been able to work hard during past year. For several months had had a dry cough; slight impairment of vision. In March friends noticed pallor. April 4, 1915, pains in lower lumbar region with fainting and dizziness.

Physical Examination.—April 11th, patient was pale and sallow. Looked sick. Conjunctiva edematous. Face puffy. Teeth bad. Lungs showed signs of chronic bronchitis and passive congestion, especially posteriorly. Sibilant and sonorous râles. Heart sounds of poor muscular quality. Presystolic thrill and systolic murmur over apex, the latter transmitted to the back. Aortic second somewhat accentuated. Pulse regular in rate and rhythm, and of fair force. Liver two finger' breadths below umbilicus. Spleen not felt, but area of dulness increased. April 15, red cells, 1,800,000; hemoglobin, 40 per cent.; polymorphonuclears, 56; transitionals, 16; lymphocytes, 16; large mononuclears, 8; eosinophils, 2.5; mast cells, 1.5; megaloblasts, 2. Respirations, 20. April 26, patient put in calorimeter. Felt better than on admission. Not strong enough to work. Lemon tinted color. Eyelids puffy. Could walk up one flight of steps without stopping. May 4, blood pressure: systolic, 130; diastolic, 80. May 10, no complaints. Discharged. (Urine showed faint trace albumin; occasional casts, and numerous leukocytes.)

DISCUSSIONS OF RESULTS

The average figures for the normal metabolism have been given in the thirteenth paper of this series.

In pernicious anemia we have obtained an increase of metabolism in all of the five cases. The figures vary from 2 to 33 per cent. above the average normal. The highest heat production was found in

Martin C. (Case 3). Unfortunately his temperature was a trifle above the normal, and he was also a little restless during this observation, as is indicated by the work-adder, the readings of which were 25, 22 and 31 for the first, second and third hours, respectively. A reading of 7 cm. is equivalent to turning from back to side. A correction of at

TABLE 1.—DETAILS OF—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Case 1 (Daniel V.)	Prelim.	9:40	.....	.....	.....	.....	.....	.....	.....
3/9/15 61.35 Kg.	1	10:40	23.22	20.55	0.822	30.86	0.323	68.82	59.74
	2	11:40	24.06	22.18	0.789	31.86	0.323	73.71	63.92
	3	12:40	24.05	21.89	0.799	32.40	0.323	72.92	65.51
Case 2 (And. K.)...	Prelim.	10:55	.....	.....	.....	.....	.....	.....	.....
3/11/14 52.72 Kg.	1	11:55	25.84	22.53	0.834	22.16	0.519	75.38	63.18
	2	12:55	25.45	21.91	0.845	25.33	0.519	73.47	72.61
Andrew K.	Prelim.	10:45	.....	.....	.....	.....	.....	.....	.....
3/27/14 52.03 Kg.	1	11:45	23.55	20.60	0.831	28.54	0.307	69.21	73.40
	2	12:45	24.60	21.30	0.840	28.55	0.307	71.75	72.89
Case 3 (Martin C.)	Prelim.	.....	.....	.....	.....	.....	.....	.....	.....
1/29/15 47.80 Kg. 1.49 Sq. M.	1	12:02	26.13	23.62	0.805	22.67	0.364	78.68	69.35
	2	1:02	24.04	22.66	0.772	27.44	0.560	74.49	76.01
	3	2:02	26.57	24.64	0.784	31.76	0.560	81.43	79.65
Martin C.	Prelim.	.....	.....	.....	.....	.....	.....	.....	.....
5/4/15 44.21 Kg 1.44 Sq. M.	1	12:16	22.02	19.12	0.838	27.39	0.237	64.41	60.69
	2	1:16	20.66	16.87	0.891	25.61	0.237	57.53	55.93
Case 4 (Bart. D.)..	Prelim.	.....	.....	.....	.....	.....	.....	.....	.....
3/15/15 41.80 Kg. 1.39 Sq. M.	1	12:18	16.28	13.76	0.861	16.01	0.224	46.55	52.47
	2	1:18	16.68	15.27	0.796	17.06	0.224	50.79	53.64
	3	2:18	17.65	15.41	0.833	16.65	0.224	51.84	51.23
Case 5 (Daniel O.)	Prelim.								
4/26/15 60.05 Kg. 1.66 Sq. M.	1	12:30	21.64	20.57	0.765	31.38	0.398	67.80	40.68
	2	1:30	22.80	21.55	0.769	31.30	0.398	71.06	46.39

least 10 per cent. is therefore necessary to account for these two factors.

Only in Cases 2 and 3 (Andrew K., and Martin C.) did the heat production exceed the range of normal variation. Both are examples of severe anemia from the clinical point of view, with a hemoglobin

percentage of less than 25. It is of interest to note that Martin C. had practically lost the use of his legs, and that his extremities were wasted and atrophic as the result of a transverse myelitis.

Bartolo D. and Daniel O. (Cases 4 and 5) cannot be said to show a pathologic increase of metabolism. It is not likely that the insuf-

—Calorimeter Experiments

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks Surface Area Meeh's Formula
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M.	
.....	37.10	...	....	.....	..	..	..	.....	.....	Basal; Sq. M. = 1.915
65.42	37.22	...	....	0.824	12	53	35	1.12	35.94	Very quiet; slept most of time
67.73	37.30	...	....	0.787	12	64	24	1.20	38.49	Slightly restless
70.15	37.40	...	....	0.798	12	60	28	1.19	38.08	Restless
.....	37.13	...	....	.....	..	..	..	.....	.....	Basal; Sq. M. = 1.731
67.18	37.23	102	14.7	0.842	18	44	38	1.43	43.55	
77.47	37.35	103	43.8	0.855	19	40	41	1.38	42.44	
.....	37.30	...	....	.....	..	..	..	.....	.....	Basal; Sq. M. = 1.706
66.57	37.15	101	34.6	0.835	12	49	39	1.33	40.57	Asleep most of 1st period
72.55	37.15	98	41.0	0.845	11	47	42	1.38	42.06	Asleep half of 2d period; restless in sleep
.....	37.90	...	....	.....	..	..	..	.....	.....	Basal; Sq. M. = 1.622
76.59	38.06	107	24.5	0.800	12.3	59.7	28.0	1.015	48.51	Somewhat restless
75.59	38.05	104	22.0	0.760	19.9	65.3	14.8	0.961	45.93	Restless 5 min.
77.43	38.01	105	31.7	0.740	18.4	72.1	9.05	1.041	49.77	Restless 5 min.
.....	.....	...	....	.....	..	..	..	.....	.....	Basal; Sq. M. = 1.539 (M)
59.35	36.60	91	24.0	0.841	9.4	49.1	41.2	1.301	.....	Fairly quiet; voided
55.73	36.60	88	6.0	0.902	10.7	30.3	58.8	1.457	.....	Very quiet
.....	37.24	...	....	.....	..	..	..	.....	.....	Basal; Sq. M. = 1.483
52.24	37.24	71	7.0	0.869	12.7	38.6	48.7	1.114	31.39	Very quiet
50.94	37.23	67	12.0	0.793	11.7	53.1	25.2	1.215	34.25	Quiet
53.03	37.20	69	6.0	0.837	11.4	48.2	40.4	1.240	34.96	Quiet
.....	.....	...	....	.....	..	..	..	.....	.....	Basal
61.08	37.04	78	15.0	0.757	15.6	68.9	15.5	1.129	35.91	Quiet
62.64	37.00	76	16.0	0.763	14.8	69.5	15.7	1.183	37.64	Quiet

ficiency of the mitral valve in Daniel O.'s case could in any way have affected his metabolism. Clinically the condition of these two patients was not so severe. Their hemoglobin approximated from 40 to 44 per cent. of the normal. Daniel O. was able to walk up one flight of steps without stopping on the day of the observation.

TABLE 2.—Summary of Calorimeter Experiments; Averages of Periods; All Basal Experiments on Men

Subject and Date	Weight, Kg.	Age, Yrs.	Aver. Calories per Hour, Indirect	Indirect Calorimetry Average per Hour							Total Calories each Experiment		Per Cent. of Divergence of Direct from Indirect	Remarks
				Average R. Q.	Average Calories per Kg.	Per Sq. M. Meeh's Formula	Per Cent. Divergence from Average Normal Basal Meeh	Average Normal Basal Meeh	Per Sq. M. Linear Formula	Per Cent. Divergence for Average Normal Basal Lin.	Average Normal Basal Lin.	Indirect	Direct		
Case 1 (Daniel V.) 5/9/13	61.35	21	71.81	0.803	1.17	37.50	+ 8	34.7	.....	.....	39.7	215.45	203.30	− 5.5	Slightly restless
Case 2 (Andrew K.) 3/11/14	52.72	27	74.42	0.839	1.41	42.99	+24	34.7	.....	.....	39.7	148.85	144.65	− 2.8	Fairly quiet
3/27/14	52.03	27	70.48	0.835	1.36	41.31	+19	34.7	.....	.....	39.7	140.96	139.12	− 1.3	Asleep
Case 3 (Martin C.) 1/29/15	47.80	32	78.20	0.787	1.636	48.21	+40.1	34.7	52.59	+32.5	39.7	231.60	229.61	− 2.1	Slightly restless
5/ 4/15	44.21	32	60.97	0.865	1.379	39.62	+ 14.2	34.7	42.43	+ 6.9	39.7	121.94	115.08	− 5.3	Quiet
Case 4 (Bartolo D.) 3/15/15	41.80	50	49.73	0.830	1.189	33.53	+ 8.8	30.8	35.91	+ 2.0	35.2	149.18	156.21	+ 4.8	Quiet
Case 5 (Daniel O.) 4/26/15	60.05	38	69.43	0.767	1.456	36.78	+ 6.0	34.7	41.90	+ 5.5	39.7	138.86	123.72	− 10.9	Quiet
												1,149.84	1,111.69	−3.3	

Daniel V. (Case 1) is a case of splenic anemia with congenital syphilis. At present we do not know what bearing the history of syphilis has in this connection.

The literature affords considerable evidence that the methods of direct and indirect calorimetry may show remarkable agreement. This agreement has been shown by Rubner and Lusk on dogs; by Atwater and Benedict on man; by Carpenter and Murlin on parturient women, and by Howland on babies. Gephart and Du Bois,[14] in their study of normal men, found that the totals of indirect and direct heat production came within 0.17 per cent. of each other, and that even in one hour periods the agreement was striking.

It is of the utmost importance to determine whether the same agreement can be demonstrated in disease. Coleman and Du Bois,[16] in their series of sixty experiments on typhoid patients, obtained an average divergence in individual experiments of 5 per cent., and a total divergence of 2.2 per cent.

In our series of anemic patients (Table 2) the total divergence between direct and indirect calorimetry is about 3.3 per cent. In three of the observations the variation is from 1 to 3 per cent. The greatest discrepancy is 12 per cent. In hourly periods the least divergence is 1 per cent., the greatest 12 per cent. In the total there were seventeen one hour periods. In ten of these periods the two methods agreed within 2.5 per cent.; in two, within 8 per cent.; in four, within from 10 to 12 per cent.

The relationship between the volume of carbon dioxid produced and the volume of oxygen consumed justifies the inference that there is no profound qualitative change in the metabolism of pernicious anemia. There is no evidence of increased protein consumption. The nonprotein respiratory quotients vary from 0.76 to 0.87, indicating that fat and carbohydrate are burned to the same end-products as in health.

In Table 3 we have tabulated the results obtained by others in a variety of anemias. In all cases in which the heat production was not given, we have converted the oxygen consumption per kilogram per minute into calories per square meter per hour, on the assumption that 15 per cent. of the calories are derived from protein. The area of body surface was computed according to Meeh's formula. We have indiscriminately applied the normal figure 34.7 calories per square meter per hour to all observations in arriving at the percentage increase or decrease in metabolism except in our own cases, in which the linear formula standards have been used in all cases measured by this method. The standard normal of 34.7 is not strictly accurate,

16. Coleman, Warren, and Du Bois, E. F.: Clinical Calorimetry, Seventh Paper, Calorimetric Observations on the Metabolism of Typhoid Patients With and Without Food, The Archives Int. Med., 1915, xv, 887.

TABLE 3.—Summary of Results of Various Investigators

Observer	Disease	Patient	Sex*	Age, Years	Weight, Kg.	Temperature	Pulse	Resp.	Hb, per Cent.	R. Q.	Calories per Sq. M per Hour Meeh's Formula	Per Cent. Above or Below Normal	Remarks
Grafe, E.	Lymph. Leuk.	T. S. 1a	♂	50	66.0	36.2	100	36	..	0.700	68.66	+98	Very dyspneic; restless at times
Grafe, E.	Lymph. Leuk.	T. S. 1b	♂	50	67.8	36.4	100	32	..	0.840	52.00	+50	
Grafe, E.	Lymph. Leuk.	T. S. 1c	♂	50	68.5	36.5	90	34	..	0.831	48.66	+40	
Grafe, E.	Lymph. Leuk.	G K. 2	♂	56	75.0	36.2	80	22	..	0.881	36.75	+ 6	
Grafe, E.	Lymph. Leuk.	G. L. 3a	♀	65	48.2	36.0	80	20	..	0.898	44.45	+28	Asleep most of time
Grafe, E.	Lymph. Leuk.	G. L. 3b	♀	65	48.0	36.2	88	24	..	0.820	46.92	+35	Asleep most of time
Grafe, E.	Lymph. Leuk.	M. T. 4	♂	49	63.8	37.2	82	22	..	0.851	65.04	+87	Restless now and then
Grafe, E.	Lymph. Leuk.	M. D. 5	♂	56	65.8	36.6	88		..	0.807	49.83	+44	
Magnus Levy	Lymph. Leuk.	J.	♂	49	53.5	....	..	..	..	0.783	45.13	+30	Av. 3 observations
Grafe, E.	Myel. Leuk.	F. N. 6	♀	32	64.3	36.6	82	20	..	0.783	53.20	+53	
Grafe, E.	Myel. Leuk.	M. H. 7	♀	38	51.0	36.7	86	18	..	0.777	49.79	+43	
Grafe, E.	Myel. Leuk.	H. B. 8	♂	48	57.5	36.5	80	15	..	0.814	42.33	+22	
Kraus, F.	Spl. Med. Leuk.	M. B	♂	60	55.0	Normal	86	12	50	0.790	48.67	+40	
Kraus, F.	Spl. Med. Leuk.	M. B.	♂	60	55.0	Normal	86	12	50	0.772	46.40	+33	
Kraus, F.	Spl. Med. Leuk.	M. B	♂	60	55.0	Normal	86	12	50	0.777	45.83	+32	
Kraus, F.	Spl. Med. Leuk.	W. K.	♂	37	74.7	Normal	100-108	14	45	0.811	47.80	+38	
Kraus, F.	Spl. Med. Leuk.	W. K	♂	37	74.7	Normal	100-108	14	45	0.814	46.72	+35	
Kraus, F.	Spl. Med. Leuk.	W K	♂	37	74.7	Normal	100-108	15	45	0.805	49.37	+42	
Kraus, F.	Splenic Leuk.	S. W.	♀	34	61.0	Normal	80	14	45-50	0.866	49.74	+43	
Kraus, F.	Splenic Leuk.	S. W	♀	34	61.0	Normal	80	12	45-50	0.808	49.17	+42	
Bohland	Splenic Leuk.	H.	♀	38	53.5	Normal	114-120	22-24	—	0.800	51.84	+49	6:30 N
Bohland	Splenic Leuk.	H.	♀	38	53.5	Normal	114	22-26	—	0.890	57.80	+66	6:15 N
Bohland	Splenic Leuk.	H.	♀	38	53.5	Normal	108	20-23	—	0.840	56.71	+63	6:45 N
Bohland	Splenic Leuk.	H.	♀	38	53.5	Normal	112-116	19-23	—	0.810	54.80	+58	10:00 N
Kraus, F.	Chlorosis	V. H.	♀	20	49.0	Normal	78-84	16	45	0.710	41.17	+19	
Kraus, F.	Chlorosis	V. H	♀	20	49.0	Normal	78-84	18	45	0.735	44.29	+28	
Magnus-Levy	Chlorosis	I. G	♀	20	44.8	....	..	..	..	0.806	34.01	- 0.2	13 observations

Magnus-Levy.....	Chlorosis.....	M. W.	♀	18	53.5	....	..	.	..	0.794	36.68	+ 7	8 observations
Thiele and Nehring .	Chlorosis..	R.	♀	22	57.5	Normal	80	12	85	0.902	31.76	— 8	Chr. otitis media
Thiele and Nehring..	Chlorosis....	R.	♀	22	57.5	Normal	80	12	85	0.805	31.21	—10	Chr. otitis media
Thiele and Nehring.	Chlorosis..... ...	R.	♀	22	57.5	Normal	80	13	85	0.858	31.97	— 8	Chr. otitis media
Thiele and Nehring..	Chlorosis...	P.	♀	18	58.5	Normal	90-100	18	55	0.925	27.98	- 19	
Thiele and Nehring..	Chlorosis	P.	♀	18	58.5	Normal	90-100	18	55	0.800	27.89	- 19	
Thiele and Nehring.	Chlorosis..... ..	P.	♀	18	58.5	Normal	90-100	24	55	0.804	28.61	- 17	Complained of toothache
Thiele and Nehring..	Chlorosis.....	P.	♀	18	58.5	Normal	90-100	24	55	0.779	29.63	15	Complained of toothache
Thiele and Nehring..	Chlorosis.... . ..	P	♀	18	59.0	Normal	90-100	20	55	0.825	28.84	- 17	
Thiele and Nehring..	Chlorosis.....	P.	♀	18	59.0	Normal	90-100	20	55	0.806	29.03	- 16	
Kraus, F.	Sec. anemia.....	L. S.	♂	33	61.0	Normal	88-100	13	25	0.752	40.73	+17	
Kraus, F.	Sec. anemia.....	L. S.	♂	33	61.0	Normal	88-100	14	25	0.763	39.48	+14	
Kraus, F.	Sec. anemia.....	L. S.	♂	33	61.0	Normal	88-100	14	25	0.746	43.99	+27	
Magnus-Levy.....	Sec. anemia.....	G. S.	♀	30	44.1	....	..	..	..	0.860	33.77	- 3	2 observations
Magnus-Levy.....	Sec. anemia.....	W. R.	♂	40	63.4	....	..	..	..	0.779	37.27	+ 7	4 observations
Magnus Levy.....	Sec. anemia...	B. L.	♀	27	47.7	....	..	..	..	0.775	30.53	- 12	8 observations
Thiele and Nehring..	Sec. anemia.....	B.	♀	—	47.5	Normal	--	19	—	0.877	35.59	+ 3	Very anemic after hemorrhoid bleeding; slept part of time
Thiele and Nehring..	Sec. anemia.....	B.	♀		47.5	Normal	--	18	—	0.850	34.53	0.5	
Thiele and Nehring..	Sec. anemia.....	B.	♀		47.5	Normal	—	17	-	0.864	36.41	+ 5	Slept part of time
Kraus, F.	Pernicious anemia	A. D	♀	46	54.0	Normal	96-108	14	30	0.710	37.52	+ 8	
Kraus, F.	Pernicious anemia	A. D.	♀	46	54.0	Normal	96-108	15	30	0.709	40.55	+17	
Magnus-Levy... ...	Pernicious anemia	M.	♀	40	44.7	....	..	..	..	0.813	38.87	+12	6 observations
Magnus-Levy... .. .	Pernicious anemia	W.	♀	45	42.5	....	..	..	..	0.738	36.17	+ 4	1 observation
Authors..... ...	Pernicious anemia, splenic	1 (D. V.)	♂	21	61.35	37.95	96	20	25	0.803	37.50	+ 8	
Authors..	Pernicious anemia	2 (A. K.)	♂	27	52.72	37.25	100-124	24-28	20	0.839	42.99	1 24	
Authors.....	Pernicious anemia	2 (A. K.)	♂	27	52.03	37.70	100-124	24-28	20	0.835	41.31	1 19	
Authors...	Pernicious anemia	3 (M. C.)	♂	32	47.80	38.00	100-124	20-30	23	0.787	48.07	1 33	
Authors.....	Pernicious anemia	3 (M. C.)	♂	32	44.21	36.00	72-115	20-24	21	0.865	39.61	+ 7	
Authors.....	Pernicious anemia	4 (B. D.)	♂	50	41.80	37.30	80-100	18-21	44	0.830	33.53	+ 2	
Authors.....	Pernicious anemia	5 (D. O.)	♂	38	60.05	37.02	..	..	40	0.767	36.78	+ 6	

* In this column ♂ denotes male; ♀, female

inasmuch as many of the subjects were women. In sixty-eight women, Benedict, Emmes, Roth and Smith found the heat production to be 32.2 calories per square meter per hour, or 7 per cent. lower than in men.

It will be observed that Magnus-Levy[12] and Kraus[9] found the metabolism in pernicious anemia from 4 to 17 per cent. above the normal. The correction for sex would increase the percentage in the case of Magnus-Levy, but would leave it unaffected in the case of Kraus, because his subjects sat on a chair, a posture which sometimes raises the metabolism.

It is interesting to notice the striking contrast between the metabolism of pernicious anemia and that of leukemia. Both Bohland[10] and Kraus[9] were led to erroneous conclusions regarding the metabolism of leukemia. This is to be explained by the fact that Bohland allowed a variation of over 30 per cent. from the average consumption of oxygen of a normal individual at rest. Kraus' upper physiologic limit of 5.75 c.c. oxygen per minute is rather high. If we interpret their results with reference to the modern base line in terms of heat units, their leukemic patients show a marked rise of metabolism. Bohland, who used the Zuntz-Geppert apparatus, states that all of his experiments were performed from five to six hours after the midday meal, or from three to four hours after breakfast, or else in the morning in a "nüchtern" state. Three of the observations which we have tabulated came between 6 and 7 in the evening and one at 10 o'clock in the morning, so that in all four the metabolism was still affected by the previous ingestion of food. Kraus, who also employed the Zuntz-Geppert method, allowed his patients to sit upright on a chair. This in itself would doubtless elevate the metabolism somewhat.

Grafe[13] used a modified form of the Jaquet apparatus in his experiments on leukemic patients. Eliminating those experiments, in which the subject was dyspneic and very restless, we obtain figures from 6 to 50 per cent. above the normal of 34.7.

Kraus,[9] Magnus-Levy[12] and Thiele and Nehring[11] have investigated chlorosis and secondary anemia. When we express the oxygen absorption which Kraus found in chlorosis, and secondary anemia in terms of calories, the metabolism is abnormally high. We must again remember that Kraus permitted his patients to sit during the observation. Magnus-Levy's results do not exceed the normal bounds. In the work of Thiele and Nehring we meet for the first time a lowered metabolism in an anemic state, although they, themselves, believed that a diminution in the oxygen intake could not be demonstrated in chlorosis.

COMPENSATORY FACTORS IN ANEMIA

It is clear from the foregoing experimental results that a reduction in the hemoglobin does not preclude the possibility of either a normal or an augmented metabolism. There is no evidence that metabolism runs its course on a lower plane in anemia. The demand for oxygen may far exceed the demand in health. How, then, is the requirement met?

In health, oxygen combines with hemoglobin by reason of chemical affinity. It is conceivable that in disease Nature may resort to physical means of increasing the combining capacity of hemoglobin. Such a conception, however, appears improbable from a comparison of Butterfield's[17] work with that of Peters.[18] Butterfield found that the ratio of CO (or O_2) : Fe averaged 399 in eleven patients, some of whom were anemic. This agrees remarkably well with the average specific oxygen capacity of 411, which Peters obtained with normal blood, using quite a different method. We may conclude that in anemia, physical means play no rôle in the absorption of oxygen apart from the slight amount taken up by the plasma in physical solution.

Normally the supply of oxygen to the tissues is beyond the immediate requirement. In anemia when the hemoglobin content is low and the volume per cent. of oxygen is correspondingly diminished, the consumption of oxygen remains normal, or may even be above the normal. Since no means of augmenting the oxygen carrying capacity per unit of blood has been demonstrated, it is manifest that the margin of safety must be encroached upon and that the blood must return to the heart in various degrees of asphyxia. That this is actually the case appears in the work of Mohr,[19] Morawitz and Röhmer[20] and Kraus and Chovstek.[21] In certain forms of anemia, under conditions of rest and with a metabolism near normal, the extra quota of oxygen which Nature has generously provided would suffice. A simple calculation, however, will show that in some patients other factors must be brought into play. Let us take, for instance, the case of Andrew K. (Case 2), whose metabolism was high and whose hemoglobin was 20 per cent. of the normal. With this amount of hemoglobin, 100 c.c.

17. Butterfield: Ueber die Lichtextinktion, das Gasbindungsvermögen und den Eisengehalt des menschlichen. Blutfarbstoffes in normalen und krankhaften Zuständen, Ztschr. f. physiol. Chem., 1909, lxii, 173.

18: Peters: Chemical Nature of Specific Oxygen Capacity in Hemoglobin, Jour. Physiol., 1912, xliv, 131.

19. Mohr: Ueber regulierende und compensirende Vorgänge im Stoffwechsel der Anämischen, Ztschr. f. exper. Path. u. Therap., 1906, ii, 435.

20. Morawitz and Röhmer: Ueber die Sauerstoffversorgung bei Anämien, Deutsch. Arch. f. klin. Med., 1908, xciv, 529.

21. Kraus and Chovstek: Ueber den Einfluss von Krankheiten auf den respiratorischen Gaswechsel, Ztschr. f. klin. Med., 1893, xxii, 573.

of blood would contain 3.7 c.c. of oxygen. Assuming a pulse rate of 70 and an average normal output per beat of 50 c.c., the minute output of oxygen would be 130 c.c. His actual need was about twice this, namely, 252 c.c. oxygen per minute as determined by the calorimeter. His pulse rate averaged 101, and therefore his output per beat must have been at least 66 c.c. to supply enough oxygen to meet the demands calculated according to the formula: Pulse Rate $\times$ Output per beat per cent. $O_2 = 252$.

Plesch[22] and Mohr[19] call attention to the increased output and pulse frequency in anemia. A more liberal supply of blood to the tissues may at times be favored by a greater respiratory volume. That the depth of respirations increase has been noticed by Jurgensen,[23] Kraus[9] and others. It is chiefly of value in facilitating the filling of the right heart. Its effect on the absorption of oxygen is negligible.

THE CAUSE OF HIGH METABOLISM IN ANEMIA

In anemia we frequently encounter signs of rapid regeneration. Normoblasts and megaloblasts may be present in secondary anemia, but are especially characteristic of pernicious anemia. Whether or not this is a reversion to the embryonic type of cell formation, the fact remains that these cells constitute a considerable mass of young tissue in the process of development. Their number in the peripheral blood is no measure of those present in the body. In the blood of rabbits with subchronic anemia experimentally induced there is a pronounced consumption of oxygen and production of carbon dioxid in vitro. This Morawitz[24] attributes to the presence of nucleated red cells.

In the leukemias we also see nucleated red cells, but their number is insignificant compared with the enormous increase in the white cells. Grafe[13] believes that the white blood cells are an important factor in the extra heat production of leukemia.

Zuntz, Löwy, Müller and Caspari[25] show that muscles poorly supplied with oxygen are functionally less efficient. Accessory muscles are called on to cooperate in the accomplishment of any task. The mechanism of the vital function of respiration and circulation becomes more complex. Proper breathing requires the activity of muscles that

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22. Plesch: Haemodynaemische Studien, Ztschr. f. exper. Path. u. Therap., 1909, vi, 526.

23. Jürgensen: In von Noorden's Pathologie der Stoffwechsel, Ed. 1, 1893, p. 335.

24. Morawitz: Ueber Oxydationsprozesse im Blut, Arch. f. exper. Path. u. Pharmakol, 1909, lx, 298.

25. Zuntz, Löwy, Müller and Caspari: Hohenklima und Bergwanderungen, Berlin, 1906, Table XII, p. 435.

ordinarily play no rôle in respiration. Again, the respiratory muscles may serve in securing a more efficient circulation. In general, activity implies unusual effort, and hence the demand for additional oxygen.

CONCLUSIONS

Three mild cases of pernicious anemia showed very slight increase in the metabolism. In two severe cases the demand for oxygen was from 7 to 33 per cent. above the normal average.

The basal metabolism of pernicious anemia is lower than that of leukemia, but, as a rule, higher than that of secondary anemia.

The agreement between the direct and indirect calorimetry as well as the respiratory quotients indicates that the basal metabolism of pernicious anemia is qualitatively identical with the normal.

Although the demand for oxygen may be increased, the compensatory processes in uncomplicated cases of pernicious anemia are capable of meeting the demand in spite of a greatly diminished hemoglobin content.

There is some ground for the belief that the height of metabolism is a measure of the severity of the clinical pictures.

477 First Avenue.

CLINICAL CALORIMETRY

SIXTEENTH PAPER

THE BASAL METABOLISM OF PATIENTS WITH CARDIAC AND RENAL DISEASE*

FRANCIS W. PEABODY, M.D.
BOSTON
A. L. MEYER, M.D., AND EUGENE F. DU BOIS, M.D.
NEW YORK
WITH THE TECHNICAL ASSISTANCE OF G. F. SODERSTROM

The literature contains extremely few reports of observations on the metabolism of patients with heart disease. The work most frequently referred to is a monograph of Kraus.[1] This study of the effect of fatigue in various pathologic conditions contains observations on the gaseous metabolism of three cardiac patients while at rest and while working on an ergograph, together with analyses of the oxygen and carbon dioxid content of the venous blood in seven cases. The metabolism experiments were made with the Zuntz apparatus. One of the most striking results is the extraordinarily low value obtained in all cases for the respiratory quotient. In the two milder cases the quotients for experiments with the subjects at rest and fasting were 0.743 and 0.603, while three similar observations in the more severe case gave as respiratory quotients 0.574, 0.534 and 0.614. Exercise brought about a rise of the quotient. In the last case exhausting work raised the quotient to 0.933 and 0.923. The blood-gas analyses showed an increase over the normal carbon dioxid content of the venous blood both at rest and during work. Kraus believed that the low respiratory quotients and the high blood carbon dioxid were best explained by assuming that one of the essential factors of the dyspnea of cardiac patients is that the lung has lost its ability to excrete carbon dioxid and take up oxygen normally, either on account of a disturbance of its glandular function (Bohr), or because of pathologic changes in the lining epithelium or the pulmonary vessels.

Grafe[2] reports observations made with the "Kopfrespirationsapparat" on the metabolism of seven patients with cardiac disease. The

* Submitted for publication Feb. 4, 1916.

* From the Russell Sage Institute of Pathology, in Affiliation with the Second Medical Division of Bellevue Hospital.

1. Kraus: Die Emüdung als ein Mass der Constitution, Bibliotheca Medica, Abt. D[1], Hefte 3, Cassel, T. G. Fisher & Co., 1897.

2. Grafe: Gaswechseluntersuchungen bei fortgeschrittenen Erkrankungen der Lungen an der Zirkulationsorgane, Deutsch. Arch. f. Klin. Med., 1909, xcv, 543.

method is open to criticism. The respiratory quotient was 0.885 in a case of congenital heart disease, 0.733 in one with Pick's cirrhosis, and 0.764 in a case of arteriosclerosis with myocarditis, but in the four other cardiac patients the quotients were remarkably low: 0.638, 0.632, 0.619 and 0.586. These instances with low respiratory quotients showed comparatively normal oxygen consumption, but low carbon dioxid production. Grafe demonstrates by calculations that it is quite impossible to accept the theory of Kraus, which accounts for the low quotients on the basis of carbon dioxid retention, as the amounts of carbon dioxid stored up in the body would be too enormous. He believes that the low respiratory quotients signify a qualitatively altered metabolism with incomplete oxidations, and suggests that the accumulation of carbon dioxid, which Kraus demonstrated by blood-gas analysis, may have injured the body protoplasm so that the chemical changes pursue an abnormal course. There seemed to be no relation between respiratory rate and increase of oxygen consumption.

While some of the respiratory quotients obtained by Grafe are so low that it is almost impossible not to suspect their accuracy, nevertheless his theory as to an altered metabolism finds some confirmation in the work of other authors who have shown that acidosis is frequently associated with cardiac disease. Thus, according to Beddard and Pembrey,[3] the alveolar carbon dioxid tension is very low in cases of decompensated cardiac disease. French, Pembrey and Ryffel[4] found it low in cases of congenital heart disease with cyanosis. Fitzgerald[5] obtained normal values for the alveolar carbon dioxid in the majority of cardiac cases, but low values in a case of mitral stenosis, and extremely low figures in a case of congenital heart disease. Porges, Leimdörfer and Markovici[6] studied a considerable series of patients with heart disease, and found that in general the carbon dioxid tension of the alveolar air is normal in those which were without dyspnea, but that it tended to be below normal in the dyspneic patients. The lowest tensions in compensated patients without dyspnea occurred in two cases of congenital heart disease, both of which probably had open ductus Botalli. Lewis[7] and his associates have shown by investigations on the blood and alveolar air that the attacks of dyspnea so commonly seen in elderly patients with renal disease or advanced arteriosclerosis are accompanied by an acidosis which they believe to be the cause of the disturbance of respiration. In cases of pure valvular

3. Beddard and Pembrey: Brit. Med. Jour., 1908, ii, 580.
4. French, Pembrey and Ryffel: Jour. Physiol., 1909, xxix, Proc., p. 9.
5. Fitzgerald: Jour. Path. and Bacteriol., 1910, xiv, 328.
6. Porges, Leimdörfer and Markovici: Ztschr. f. klin. Med., 1913, lxxvii, 446.
7. Lewis, Ryffel, Wolf, Cotton and Barcroft: Heart, 1913, v, 45. Lewis and Barcroft: Quart. Jour. Med., 1915, vii, 97.

disease with cyanosis, they found no evidence of acidosis, but that there may be an acidosis in severely decompensated cases, which disappears as compensation is regained, is shown by the observations of Porges, Leimdörfer and Markovici.[6] It is, however, particularly in the type of case which may be conveniently grouped under the heading of "cardiorenal" disease that the factor of acidosis assumes a more permanent and thus a more important part. The association of acidosis with chronic nephritis has been carefully discussed by Sellards[8] and by Palmer,[9] and its relation to the course of the disease has been studied by Peabody.[10] The significance of acidosis in investigations on metabolism was first suggested by Benedict and Joslin,[11] who showed that in two normal subjects an acidosis resulting from the administration of a carbohydrate-free diet was accompanied by an increase in the total metabolism. This observation has since been confirmed by Higgins, Fitz and Peabody.[12] Lusk believes that this increase is due to the increased protein metabolism of the carbohydrate-free periods.

METHODS USED

It is thus quite evident that in studying the metabolism of patients with heart disease it is of the utmost importance to know whether or not there is an acidosis. On account of its direct bearing on the subject of acidosis, and also on account of any other possible, but as yet unknown effects which a nephritis may exert on the metabolism, it is also of importance to know as much as possible about the functional capacity of the kidneys. At the time when the earlier of the cases reported here were investigated, renal function tests were not in general use, but the later cases were, whenever possible, studied with these points in mind. As an index of acidosis, the carbon dioxid tension of the alveolar air was determined. This was done by the Higgins modification of the method of Plesch, which has proved very satisfactory for clinical work. The normal alveolar carbon dioxid tension by this method is approximately 40 to 45 mm. In some instances the alkali tolerance test of Sellards[8] was used. The determination of the part played by the kidneys in cases of cardiac or cardiorenal disease is, of course, proverbially difficult and unsatisfactory. In general we have relied on the history, physical examination, urine examination, blood

8. Sellards: Johns Hopkins Hosp. Bull., 1912, xxiii, 289; ibid., 1914, xxv, 141.
9. Palmer: Med. Communicat., Mass. Med. Soc., 1913, xxiv, 133.
10. Peabody, F. W.: Studies on Acidosis and Dyspnea in Renal and Cardiac Disease, The Archives Int. Med., 1914, xiv, 236; Clinical Studies on the Respiration, II, The Acidosis of Chronic Nephritis, ibid., 1915, xvi, 955.
11. Benedict and Joslin: Publications of the Carnegie Institution of Washington, 1912, Pub. 176.
12. Higgins, Fitz and Peabody: Unpublished.

pressure and phenolsulphonephthalein test to aid us in differentiating the pure cardiac from the renal or cardiorenal cases.

The patients were all from the medical wards of Bellevue Hospital, but during the period of study they were kept in the special metabolism ward. The general method of conducting the observations was similar to that described in the third and fourth paper of this series.[13] The patients were usually put into the calorimeter for a short period in the afternoon, in order that they might become accustomed to the new surroundings, and then put in again for the actual experiment on the following day. As one of the chief points which we wished to investigate was the influence of dyspnea on the metabolism, quite a number of the decompensated patients were put into the calorimeter. In spite of their comparatively serious condition, however, no patient was in any way injured by his stay in it. The majority said they felt better when they came out, and, indeed, the period of absolute quiet seemed to have only a beneficial effect. The construction of the chair described in the eleventh paper made it possible to study the metabolism of patients with orthopnea. The respirations were counted by watching the patient through the glass window in the side of the calorimeter, but the graphic records registered by the spirometer on a kymograph for the five minutes at the end of each period were of help, particularly in drawing attention to periodic breathing.

DISCUSSION OF RESULTS

The total number of patients investigated was sixteen. One of these (Case 3, Fred D.) was examined first when he was decompensated and dyspneic (3a), and later when he was compensated (3b). Six cases (11, William S., 12, George M., 13, Marcus R., 14, David K., 15, William A., 16, Theodore S.) were studied for purposes not directly connected with the present investigations so that the details on them are not complete, but they are included since they serve as controls of the more severely ill patients, and contribute information about various special points. Seven cases 2, Armon W., 3, Fred D., 4, Edward M., 9, Burrell P., 11, William S., 15, William A., 16, Theodore S.) were instances of pure cardiac disease; two were cases of nephritis (12, George M., 14, David K.) and six (1, Arthur V., 5, Charles L., 7, Edward W., 8, Henry R., 10, August F., 13, Marcus R.) were mixed cases belonging to the "cardiorenal disease" group. At the time when they were in the calorimeter, five patients (1, Arthur V., 3a, Fred D., 4, Edward M., 8, Henry R., 10, August F.) had moderately severe dyspnea; seven had slight dyspnea (2, Armon W., 5,

13. Gephart, F. C., and DuBois, E. F.: The Organization of a Small Metabolism Ward, The Archives Int. Med., 1915, xv, 829; The Determination of the Basal Metabolism of Normal Men and the Effect of Food, ibid., 1915, xv, 835.

TABLE 1.—Summary of Calorimeter Experiments; Indirect Calorimetry: Averages Per Hour

Case No. and Name	Date	Age	Sex*	Indirect Calorimetry			Average per Hour		Average Normal Basal Calories per Sq. M. per Hour		Remarks
				Average Calories per Kg.	Per Sq. M., Meeh	Per Cent. Divergence from Average Normal Basal, Meeh	Per Sq. M., Linear Formula	Per Cent. Divergence from Average Normal Basal Linear	According to Meeh's Formula	According to Linear Formula	
1 Arthur V.	2/12/15	40	♂	1.57	54.4	+42	58.7	+48	34.7	39.7	Restless
2. Armon W.	2/13/15	33	♂	1.21	38.6	+11	47.7	+19	34.7	39.7	Quiet
3 Fred D.	2/15/15	17	♂	1.51	45.1	+17	53.8	+28	38.5	42.0	Very quiet
	2/23/15	..	..	1.41	38.5	0	42.7	+ 2	38.5	42.0	Very quiet
4. Edward M. ..	2/17/15	37	♂	1.18	39.5	+15	....	....	34.7	....	Restless
5. Charles L.	2/19/15	54	♂	1.08	38.7	+26	....	....	30.8	....	Quiet
6. Annie T.	2/20/15	14	♀	1.75	42.2	+10 (?)	43.9	— 5 (?)	38.5 (?)	46.4 (?)	Slightly restless
7 Edward W.	2/24/15	37	♂	1.68	51.8	+49	....	....	34.7	....	Slightly restless
8. Henry R.†	2/26/15	40	♂	1.05	36.0	+ 4	45.7†	+15†	34.7	39.7	Quiet
9. Burrell P.	3/24/15	41	♂	1.20	37.3	+ 7	48.9	+23	34.7	39.7	Restless
10. August F	5/ 1/15	62	♂	1.04	31.7	+ 3	36.9	+ 5	30.8	35.2	Quiet
11. William S.	2/10/15	48	♂	1.06	34.8	— 2	41.7	+ 8	34.7	39.7	Fairly quiet
12. George M.	4/ 7/13	56	♂	1.08	33.1	+ 8	....	....	30.8	....	Restless
	4/14/13	..	..	1.01	31.7	+ 3	....	....	30.8	....	Quiet
	3/24/14	..	..	1.03	31.1	+ 1	....	....	30.8	....	Quiet
	4/ 4/14	..	..	1.03	31.0	+ 1	....	....	30.8		
13. Marcus R.	4/ 9/13	51	♂	1.34	43.5	+41	....	....	30.8	....	Very quiet
14. David K.	3/21/13	54	♂	1.22	39.3	+28	....	....	30.8	....	Restless
	3/24/13	..	..	1.14	37.0	+20	....	....	30.8		
15. William A. ..	1/25/15	24	♂	1.13	36.3	+ 5	39.6	0	34.7	39.7	Fairly quiet
	1/27/15	..	..	1.17	37.9	+ 9	41.2	+ 4	34.7	39.7	Quiet
16. Theodore S.	1/28/14	32	♂	1.17	37.1	+ 9	45.1	+ 4	34.7	39.7	Very quiet
	1/30/14	..	..	1.10	34.8	+ 2	38.8	— 2	34.7	39.7	Very quiet
	2/ 5/14	..	..	1.15	36.7	+ 7	39.9	0	34.7	39.7	Very quiet
	2/ 9/14	.	..	1.03	33.0	— 4	37.1	— 7	34.7	39.7	Very quiet
	2/13/14	..	..	1.13	36.4	+ 7	41.1	+ 3	34.7	39.7	Very quiet

* In this column, ♂ denotes male, and ♀ female.

† In Case 8 (Henry R.) there was some error in the measurements of the height or of the surface. The three measurements of the linear formula L, O and R added together give a total length of 150 cm. from soles of feet to suprasternal notch. His height was recorded as 153 cm. According to the linear formula measurement, his surface area was 1.958 sq. m. or only 13 per cent. below the figure of 2.215 obtained by Meeh's formula. With fat individuals of his body shape the true surface is usually about 20 per cent. below the estimate according to Meeh. This would make his surface about 1.77 sq. m. According to new height-weight chart it would be 1.73. His metabolism per square meter per hour on this new basis would be about 15 per cent. above the average, or 45.70 calories per square meter.

Charles L., 6, Annie T., 7, Edward W., 9, Burrell P., 11, William S., 13, Marcus R.), and five had normal respiration (3b, Fred D., 12, George M., 14, David K., 15, William A., 16, Theodore S.).

Respiratory Quotients.—In striking contrast to the results of Kraus and Grafe, which have been described above, all of the respiratory quotients in this series of cases fell within comparatively normal limits. Our lowest quotient was 0.73 (Case 4, Edward M.). Of the ten cases reported by Kraus and Grafe, only four had respiratory quotients equal or above our lowest figure, while in the other six the results had to be explained as being caused by a qualitative alteration in metabolism. On the basis of the respiratory quotients, as obtained by us, there is no need to assume any change in the type of metabolism from the normal. In general there is a distinct tendency for the lowest quotients to be found in the cases with most dyspnea. Five patients, classed as having moderately severe dyspnea, gave as quotients: 0.74, 0.75, 0.73, 0.75 and 0.82. In seven patients with slight dyspnea the quotients were 0.79, 0.76, 0.81, 0.79, 0.84, 0.82 and 0.78, while the patients without dyspnea showed the following quotients: 0.88, from 0.80 to 0.83, from 0.74 to 0.75, from 0.81 to 0.85 and from 0.80 to 0.85 (Table 2).

DIRECT AND INDIRECT CALORIMETRY

In the previous papers of this series the close agreement between the methods of direct and indirect calorimetry with normal subjects has been demonstrated. In disease, owing to certain technical difficulties, there is a tendency for the method of direct calorimetry to average from 1 to 2 per cent. lower, particularly if short periods are used. In the group of cardiac and nephritic patients here presented, the total of the calories measured by indirect calorimetry is 4,297.67, by direct calorimetry 4,214.53, or 1.93 per cent. lower. This is remarkably good agreement, considering the technical difficulties, and indicates that there is no profound change in the metabolism which would upset calculations based on the method of indirect calorimetry.

TOTAL METABOLISM

The total metabolism is compared with the normal in terms of the heat production per square meter of surface area per hour. After the linear formula was devised, it was possible to measure most of the patients in this manner and use the results as a basis of the calculations. In all other cases it has been necessary to use Meeh's formula, which is fairly satisfactory with these subjects, since they all happened to be of about the normal body shape.

Of the five patients with moderately severe dyspnea, all but one (Case 10, August F.) showed a distinct increase in metabolism. Of

TABLE 2.—Clinical Findings and—

Case No. and Name	Age	Date in Calorimeter	Diagnosis	Blood Pressure	Pulse Rate	Phthalein Per Cent.
1. Arthur V.	40	2/12/15	Chronic nephritis, chronic myocarditis with decompensation	110-70	99	2/15=32% 2/27=63%
2. Armon W.	33	2/13/15	Double mitral disease, auricular fibrillation	110-70	77	—
3a. Fred D.	17	2/15/15	Double mitral disease, decompensation	—	105	—
3b. Fred D.	..	2/23/15	Compensated	95-70	86	—
4. Edward M.	37	2/17/15	Mitral insufficiency, auricular fibrillation, decompensation	120-85	78	—
5. Charles L.	54	2/19/15	Aortic and mitral insufficiency, chronic nephritis, emphysema	180-90	71	30%
6. Annie T.	14	2/20/15	Congenital heart disease, open ventricular septum, dextrocardia	95	102	—
7. Edward W.	37	2/24/15	Chronic nephritis, cardiac dilatation, syphilis	190-100	112	10%
8. Henry R.	40	2/26/15	Chronic myocarditis, emphysema, chronic nephritis	160-120	116	48%
9. Burrell P.	41	3/24/15	Aortic stenosis and insufficiency, mitral and tricuspid insufficiency, aneurysm of aorta	—	66	—
10. August F.	62	5/ 1/15	Chronic nephritis, auricular fibrillation	170-110(?)	77	24%
11. William S.	48	2/10/15	Adherent pericardium	110-80(?)	91	—
12. George M.	56	4/ 7/13	Chronic nephritis, cardiac hypertrophy	170-95	64	.....
		4/14/13	.....	170-55	.....	.....
		3/24/14	.....	195-115	59	.....
		4/ 4/14	.....	160-102	60	.....
13. Marcus R.	57	4/ 9/13	Chronic nephritis, mitral insufficiency, arteriosclerosis	310-160	81	.....
14. David K.	54	3/21/13	Chronic nephritis, arteriosclerosis, inguinal hernia	195-110	.....	.....
		3/24/13	.....	.....	.....	.....
15. William A.	24	1/25/15	Aortic insufficiency	140	61	.....
		1/27/15	.....	.....	66	.....
16. Theodore S.	32	1/28/14	Mitral stenosis, auricular fibrillation	.....	50	.....
		1/30/14	.....	.....	53	.....
		2/ 5/14	.....	.....	49	.....
		2/ 9/14	.....	.....	48	.....
		2/13/14	.....	145-85	55	.....

—Calorimeter Results Compared

Arterio-sclerosis (radial)	Resp. Rate	Dyspnea	Or-thop-nea	Periodic Resp.	Cyano-sis	Edema	Alveolar CO_2 Tension, mm.	R. Q.	Metab. % Deviation from Av. Norm.	
0	36	+	+	+	Slight	0	2/12=23.9 2/16=30.9 2/27=41.6	0.739	+48	
0	26-28	Slight	..	0	Slight	....	2/13=44.2	0.791	+19	
0	27-25	+	+	0	Slight	+	2/15=27.8 2/16=33.7	0.753	+28	
0	22-18	0	0	0	Slight	0	2/18=35.5 2/23=37.1	0.876	+ 2	
0	30-24	+	+	0	+	Slight	2/16=38.6	0.733	+15	
0	28-26	Slight	..	+	0	0	2/19=39.4	0.766	+26	
0	20-18	+	0	0	++	0	2/18=25.2	0.807	— 5	
+	23-21	Moderate	+	+	Slight	Slight	2/24=38.9 2/27=40.0	0.789	+49	Died, April 17, 1915
0	39-38	++	+	Slightly	—	Slight	2/25=41.1 2/26=39.9	0.747	+15	
+	25-22	Slight	+	0	—	....	—	0.837	+23	
+	28-27	+	++	+	Slight	+	—	0.815	+ 5	
..	19-18	Slight	+	0	+	....	—	0.817	+ 8	
Slight	.....	Slight	....	.....	....	±	.....	0.819	+ 8	
.....	.....	Slight	....	.....	....	+	.....	0.796	+ 3	
.....	24-18	Slight	....	.....	....	+	.....	0.827	+ 1	
.....	.....	Slight	....	.....	....	+	.....	0.815	+ 1	
++	20-18	Slight	....	.....	0	0	.....	0.781	+41	
+	.....	0	0	.....	0	0	.....	0.746	+28	
+	.....	0	0	.....	....	....	.....	0.744	+20	
.....	.....	0	0	... .	....	....	.....	0.852	± 0	Lying flat on back
.....	.....	0	0	.....	....	....	.....	0.814	+ 4	Steamer chair
0	.....	0	0	.....	+	0	.....	0.822	+ 9	Flat on back
.....	.....	0	0	.....	+	0	.....	0.831	+ 2	Sitting in bed at angle of 30°
.....	.....	0	0	.....	+	0	.....	0.803	+ 7	Lying flat on back
.....	.....	0	0	.....	+	0	.....	0.842	— 4	Sitting up at angle of 50°
.....	.....	0	0	.....	+	0	.....	0.854	+ 7	Lying flat on back

the seven with slight dyspnea, all showed an increase except the underdeveloped girl with congenital heart disease. Of the five with no dyspnea, the only one with increased metabolism was the restless and unsatisfactory alcoholic, David K. (Case 14).

Dyspneic patients must do an increased amount of muscular work in their labored breathing, but it is doubtful if this would account for an increase of 10 per cent. Some of the dyspneic patients were rest-

TABLE 3.—Patients with Moderately Severe Dyspnea, Slight Dyspnea and No Dyspnea

Subject	Case No.	Pulse	R. Q.	Per Cent. Increase of Metabolism above the Normal	Alveolar CO_2 Tension, mm.
Patients with moderately severe dyspnea					
Arthur V.	1	99	0.739	+48	23.9
Fred D.	3a	105	0.753	+28	27.8
Edward M.	4	78	0.733	+15	38.6
Henry R.	8	116	0.747	+15?	39.9
August F.	10	77	0.815	+ 5	....
Patients with slight dyspnea					
Armon W.	2	77	0.791	+19	44.2
Charles L.	5	71	0.766	+26	39.4
Annie T.	6	102	0.807	+ 5	21.7
Edward W.	7	112	0.789	+49	38.9
Burrell P.	9	66	0.837	+23	....
William S.	11	91	0.817	+ 8	....
Marcus R.	13	81	0.781	+41	....
Patients with no dyspnea					
Fred D.*	3b	105	0.753	+ 2	37.1
George M.	12	59–64	0.80-0.83	+ 1 to + 8	....
David K.	14	.....	0.74-0.75	+20 to +28	....
William A.	15	61	0.81-0.85	0 to + 4	....
Theodore S.	16	48-55	0.80-0.85	— 7 to + 4	....

* Compensated.

less while in the calorimeter, but a similar degree of restlessness in other patients does not increase the metabolism more than about 10 per cent. This factor may be of some importance in the cases of Arthur V. (Case 1), Edward M. (Case 4), Edward W. (Case 7), Burrell P. (Case 9) and David K. (Case 14), but other patients with high metabolism for example, Armon W. (Case 2), Fred D. (Case 3), Charles L. (Case 5), Henry R. (Case 8) and Marcus R. (Case 13) were as quiet as the normal controls. It is evident that most dyspneic

patients show a metabolism increased from some cause other than muscular activity.

An analysis of the relation between increase of metabolism in these cases and acidosis is of considerable interest. It is unfortunate that the carbon dioxid tension of the alveolar air was not determined in all the patients. The lowest carbon dioxid was found in Case 6 (Annie T.), but it is quite possible that in such a case of congenital heart disease the decreased alveolar carbon dioxid might not be accurate evidence of the change in the reaction of the blood. Excluding this patient, the two with the lowest carbon dioxid, Arthur V. (Case 1) and Fred D. (Case 3) showed marked increase in metabolism. Still there were two others with high metabolism (Edward W., Case 7, and Charles L. Case 5) whose alveolar carbon dioxid was very slightly depressed.

It is interesting to note that patients with low excretion of phenolsulphonephthalein, Arthur V. (Case 1), Charles L. (Case 5) and Edward W. (Case 7), showed marked increase in metabolism; but one, August F. (Case 10), whose phenolsulphonephthalein was low, showed no increase.

Six patients gave systolic blood pressure readings of 170 mm. or over. Of these four, Charles L. (Case 5), Edward W. (Case 7), Marcus R. (Case 13) and David K. (Case 14) had high metabolism, while two, August F. (Case 10) and George M. (Case 12), had low metabolism.

It is evident that in so complex a group of subjects as the sixteen cardiacs and nephritics, there are many factors at work. At present it would seem as if no one factor would account for the definite increase in metabolism found in the dyspneic patients. The studies in this subject are being continued.

It is of interest to note that patients with compensated cardiac lesions or with mild nephritis show a metabolism within the normal limits.

SUMMARY AND CONCLUSIONS

Sixteen patients with cardiac and cardiorenal disease have been studied, and for the first time the methods of direct and indirect calorimetry have been compared. In this group of cases the two methods have been found to agree within 1.9 per cent.

The respiratory quotient in all cases was within normal limits (0.73 or above). This is opposed to the findings of Kraus and Grafe. The normal quotients and the very close agreement of the direct and indirect calorimetry prove that there is no profound change in the intermediary metabolism.

TABLE 4.—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Case 1 (Arthur V.)	Prelim.	11:19	.....	.....	.....	.....	.....	.....	.....
2/12/15									
58.26 Kg.	1*	12:22	30.05	29.35	0.75	49.92	0.331	96.62	94.96
1.556 Sq. M.	2†	1:19	26.41	26.26	0.73	48.47	0.331	85.99	88.82
								182.61	
Case 2 (Armon W.)	Prelim.	11:25	.....	.....	.....	.....	.....	.....	.....
2/13/15									
60.77 Kg.	1	12:25	24.11	21.73	0.81	27.78	0.266	72.69	72.61
1.550 Sq. M.	2	1:25	23.85	22.37	0.78	28.32	0.266	74.15	71.81
								146.84	
Case 3 (Fred D.)...	Prelim.	11:34	.....	.....	.....	.....	.....	.....	.....
2/15/15									
49.75 Kg.	1	12:34	23.37	22.54	0.75	36.61	0.579	73.75	76.63
1.394 Sq. M.	2	1:34	24.07	23.30	0.75	37.44	0.579	76.27	78.63
								150.02	
Fred D.	Prelim.	11:19	.....	.....	.....	.....	.....	.....	.....
2/23/15									
39.68 Kg.	1	12:19	19.07	14.77	0.94	24.00	0.331	50.76	56.63
1.291 Sq. M.	2	1:19	20.53	16.90	0.88	25.27	0.331	57.38	60.43
	3§	1:49	9.82	8.87	0.81	12.48	0.331	29.56	29.00
								137.70	
Case 4 (Edw. M.)..	Prelim.	11:30	.....	.....	.....	.....	.....	.....	.....
2/17/15									
68.88 Kg.	1	12:30	23.35	23.41	0.76	36.73	0.399	76.37	89.58
	2	1:30	26.87	26.37	0.74	36.51	0.399	86.49	90.02
								162.86	
Case 5 (Chas. L.)	Prelim.	11:25	.....	.....	.....	.....	.....	.....	.....
2/19/15									
85.84 Kg.	1	12:25	28:50	27.18	0.76	35.43	0.287	89.96	89.41
	2	1:25	30.50	28.84	0.77	39.05	0.287	95.71	93.28
								185.67	
Case 6 (Annie T.)..	Prelim.	10:57	.....	.....	.....	.....	.....	.....	.....
2/20/15									
26.27 Kg.	1	11:57	15.29	13.69	0.81	20.09	0.150	45.83	43.83
1.046 Sq. M.	2	12:57	15.20	13.78	0.80	20.78	0.150	46.02	43.80
								91.85	
Case 7 (Edw. W.)..	Prelim.	11:18	.....	.....	.....	.....	.....	.....	.....
2/24/15									
54.35 Kg.	1	12:18	28.90	26.69	0.79	47.27	0.357	88.64	89.35
	2	1:18	30.78	28.29	0.79	47.66	0.357	94.21	94.88
								182.85	
Case 8 (Henry R.)	Prelim.	11:32	.....	.....	.....	.....	.....	.....	.....
2/26/15									
75.49 Kg.	1	12:32	24.62	24.07	0.74	38.36	0.303	79.21	77.35
1.73(?) Sq. M.	2	1:32	24.75	23.98	0.75	40.81	0.303	78.91	80.88
								158.12	

* 63 min. † 57 min. § 30 min.

—Calorimeter Experiments

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M.	
.....	37.61									
94.15	37.60	100	37.2	0.74	9	80	11	1.66	52.23	Restless period 63 min.
81.51	37.46	97	45.0	0.72	10	86	4	1.48	46.48	Restless period 57 min.
175.66										
.....	36.99									
72.78	37.00	76	14.2	0.81	10	58	32	1.20	38.19	Quiet; reading 40 min.
71.50	37.00	78	30.3	0.77	10	71	20	1.22	38.96	Quiet; reading 5 min.
144.28										
.....	38.17									
74.63	38.15	104	5.0	0.74	21	70	9	1.48	44.29	Very quiet
76.00	38.11	105	14.0	0.74	20	71	9	1.53	45.81	Very quiet
150.63										
.....	36.83									
56.41	36.83	86	5.0	0.97	17	8	74	1.28	35.45	Asleep 40 min.
55.16	36.68	81	7.0	0.90	15	29	56	1.45	40.07	Very quiet
29.54	36.70	91	4.0	0.81	15	55	30	1.49	41.28	Very quiet
141.11										
.....	36.99									
80.00	36.83	80	41.5	0.71	14	85	1	1.11	37.08	Very restless
92.59	36.88	76	38.0	0.73	12	81	7	1.26	42.00	Restless
172.59										
.....	37.15									
86.23	37.11	70	23.6	0.76	8	75	17	1.05	37.55	Quiet, dozing and reading
96.41	37.16	71	25.0	0.77	8	72	20	1.12	39.95	Quiet, reading
182.64										
.....	37.16									
42.07	37.09	102	24.0	0.81	9	59	32	1.74	42.12	Restless
44.23	37.12	102	16.0	0.80	9	62	29	1.75	42.30	Fairly quiet
86.30										
.....	37.55									
80.94	37.37	111	25.0	0.79	11	66	23	1.63	50.19	Fairly quiet; dozing
97.28	37.46	112	32.0	0.79	10	64	26	1.73	53.35	Slightly restless
178.22										
.....	37.40									
76.49	37.39	117	21.0	0.74	10	79	10	1.05	36.02	Quiet
75.94	37.32	115	13.0	0.74	10	79	10	1.05	35.88	Quiet
152.43										

TABLE 4.—CALORIMETER—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Case 9 (Burrell P.)	Prelim.	11:10	.....	.....	.....	.....	.....	.....	.....
3/24/15									
70.81 Kg.	1	12:10	30.31	27.06	0.82	33.75	0.544	90.29	88.94
1.739 Sq. M.									
	2	1:10	27.96	23.67	0.86	29.89	0.544	79.67	86.20
								169.96	
Case 10 (Aug. F.)	Prelim.	12:00	.....	.....	.....	.....	.....	.....	.....
5/1/15								Approx.	
52.61 Kg.	1	1:00	18.26	15.49	0.86	25.98	.....	52.50	49.62
1.487 Sq. M.									
	2	2:00	18.38	17.29	0.77	25.55	.....	57.27	51.67
								109.77	
Case 11 (Wm. S.)..	Prelim.	11:29	.....	.....	.....	.....	.....	.....	.....
2/10/15									
65.02 Kg.	1	12:29	22.68	19.76	0.84	22.48	0.515	65.97	65.29
1.62 Sq. M.									
	2	1:29	23.75	21.83	0.80	24.97	0.515	72.40	71.41
								138.37	
Case 12 (Geo. M.)	Prelim.	10.00	.....	.....	.....	.....	.....	.....	.....
4/7/13									
54.29 Kg.	1	12:00	40.29	34.52	0.85	45.15	0.392	115.92	104.16
	2	2:00	38.76	35.64	0.79	49.34	0.392	118.02	115.02
								233.94	
George M.	Prelim.	10:00	.....	.....	.....	.....	.....	.....	.....
4/14/13									
57.18 Kg.	1	12:00	36.23	32.33	0.82	46.23	0.311	107.87	101.38
	2	2:00	39.98	37.36	0.78	49.48	0.311	123.66	112.01
								231.53	
George M.	Prelim.	11:36	.....	.....	.....	.....	.....	.....	.....
3/24/14									
58.82 Kg.	1	12:36	19.31	16.27	0.86	23.14	0.385	54.85	61.59
	2	1:36	20.08	18.44	0.79	25.03	0.385	61.10	65.68
								115.95	
George M.	Prelim.	11:40	.....	.....	.....	.....	.....	.....	.....
4/4/14									
58.98 Kg.	1	12:50	22.70	21.12	0.78	26.32	0.402	69.74	63.87
	2	1:40	16.14	13.84	0.85	18.94	0.402	46.44	46.38
								116.18	
Case 13 (Marcus R.)	Prelim.	10:00	.....	.....	.....	.....	.....	.....	.....
4/9/19									
63.43 Kg.	1	12:00	55.21	52.33	0.77	68.56	0.456	172.64	148.96
	2	2:00	55.27	50.59	0.80	74.22	0.456	168.03	162.03
								340.67	
Case 14 (David K.)	Prelim.	9:40	.....	.....	.....	.....	.....	.....	.....
3/21/13									
62.66 Kg.	1	10:40	25.86	25.55	0.74	32.26	0.323	83.84	79.94
	2	11:40	21.78	20.91	0.76	28.71	0.323	68.89	66.49
								152.73	
	3	12:40	27.13	26.95	0.73	32.44	0.323	88.36	82.37
	4	1:40	29.35	27.43	0.78	32.74	0.323	91.04	84.88
	5	2:40	25.50	23.78	0.78	30.95	0.323	78.89	80.54
	6	3:40	23.74	23.61	0.73	30.16	0.323	77.32	79.79
								488.34	

—EXPERIMENTS—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
.....	37.87									
79.78	37.72	68	36.0	0.82	16	51	33	1.30	39.67	Restless
81.04	37.64	64	35.0	0.87	18	36	46	1.13	35.01	Restless
160.82										
.....	38.18									
45.76	38.10	78	12.0	....	..	..	..	....	.....	Very quiet; asleep 15 min.
51.43	38.10	76	7.0	....	..	..	..	....	.....	Quiet
97.19										
.....	36.79									
59.13	36.68	85	3.0	0.84	21	43	36	1.02	33.13	Very quiet
71.16	36.71	98	27.6	0.80	19	55	26	1.11	36.36	Restless
130.29										
.....	36.52									
112.80	36.72	64	....	0.86	18	40	42	1.07	32.84	Restless
117.72	36.79	...	....	0.79	18	59	23	1.09	33.43	Restless
230.52										
.....	36.78									
96.03	36.66	...	....	0.82	15	53	32	0.94	29.52	Asleep
115.88	36.76	...	....	0.77	13	67	20	1.08	33.84	Slightly restless
211.91										
.....	36.68									
50.97	36.47	58	14.9	0.88	19	34	47	1.02	29.46	Asleep 30 min.
63.66	36.47	60	21.3	0.79	17	59	24	1.04	32.81	Asleep 10 min.
114.63										
.....	36.53									
64.04	36.54	59	29.8	0.78	18	62	20	1.01	32.04	
50.94	36.64	60	9.0	0.86	19	39	42	0.94	29.87	
114.98										
.....	37.24									
165.91	37.57	...	....	0.76	14	70	16	1.36	44.09	Very quiet
163.27	37.60	...	....	0.79	14	61	25	1.32	42.91	Very quiet
329.18										
.....	36.97									
82.17	37.02	...	....	0.73	10	83	7	1.34	43.26	Restless
69.16	37.06	...	....	0.75	12	75	13	1.10	35.47	Restless
151.33										
.....	37.01	...	....	0.72	10	84	6	1.41	45.49	At 11:40 a. m., oatmeal
.....	36.97	...	....	0.78	9	70	21	1.45	46.87	
.....	37.09	...	....	0.78	11	67	22	1.26	40.62	
.....	37.01	...	....	0.72	11	84	5	1.23	39.81	
155.33										

TABLE 4.—CALORIMETER—

Subject, Date, Weight, Surface Area, Linear Formula†	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
David K.	Prelim.	9:21	.....	.....	.....	.....	.....	.....	.....
3/24/13									
64.26 Kg.	1	10:21	22.91	22.75	0.73	27.51	0.391	74.39	68.85
	2	11:21	22.66	21.78	0.76	27.73	0.391	71.65	67.05
								146.04	
Case 15 (Wm. A.)..	Prelim.	11:13	.....	.....	.....	.....	.....	.....	.....
1/25/15									
63.44 Kg.	1	12:13	25.32	20.31	0.91	24.45	0.382	69.44	72.58
1.795 Sq. M.									
	2	1:13	24.08	20.86	0.84	32.15	0.382	70.14	73.06
	3	2:13	24.45	22.02	0.81	31.11	0.382	73.44	73.48
								213.02	
William A.	Prelim.	10:40	.....	.....	.....	.....	.....	.....	.....
1/27/15									
63.00 Kg.	1	11:40	24.37	21.08	0.84	32.50	0.390	70.86	73.83
1.790 Sq. M.									
	2	12:40	25.01	22.17	0.82	32.37	0.390	74.09	75.33
	3	1:40	24.75	23.05	0.78	33.53	0.390	76.38	78.06
								221.33	
Case 16 (Theo. S.)	Prelim.	11:10	.....	.....	.....	.....	.....	.....	.....
1/28/14									
59.52 Kg.	1	12:10	23.13	20.30	0.83	39.03	0.454	67.86	77.28
1.68 Sq. M.									
	2	1:10	23.98	21.43	0.81	38.26	0.454	71.40	76.66
								139.26	
Theodore S.	Prelim.	11:15	.....	.....	.....	.....	.....	.....	.....
1/30/14									
59.44 Kg.	1	12:15	21.66	18.76	0.84	36.00	0.385	62.97	73.11
1.68 Sq. M.									
	2	1:15	22.80	20.18	0.82	37.75	0.385	67.48	73.83
								130.45	
Theodore S.	Prelim.	11:46	.....	.....	.....	.....	.....	.....	.....
2/5/14									
60.28 Kg.	1*	1:16	34.63	31.59	0.80	50.61	0.538	105.10	118.65
1.69 Sq. M.									
	2	2:16	22.82	20.53	0.81	32.00	0.359	68.47	72.40
								173.57	
Theodore S.	Prelim.	11:50	.....	.....	.....	.....	.....	.....	.....
2/9/14									
61.15 Kg.	1	12:50	21.11	18 41	0.83	21.14	0.394	61.66	56.93
1.70 Sq. M.									
	2	1:50	22.34	19.11	0.85	22.55	0.394	64.30	60.88
								135.96	
Theodore S.	Prelim.	11:10	.....	.....	.....	.....	.....	.....	.....
2/13/14									
61.99 Kg.	1	12:10	24.54	20.49	0.87	26.73	0.391	69.38	70.40
1.71 Sq. M.									
	2	1:10	24.35	21.15	0.84	33.09	0.391	71.02	75.79
								140.40	

* 1½ hours. † In the case of Theodore S. the height-weight formula.

—EXPERIMENTS—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
.....	36.96									
76.52	37.11	...	....	0.72	14	82	4	1.16	37.66	
66.14	37.10	...	....	0.75	14	73	13	1.11	36.27	
142.66										
.....	36.96	..	....	....	..	..	..	....	.....	Basal; flat in bed
62.29	36.77	62	20.2	0.93	15	20	65	1.10	35.47	Restless
69.48	36.71	60	10.5	0.85	14	68	18	1.11	35.82	Fairly quiet
70.55	36.66	62	10.0	0.81	14	62	24	1.16	37.51	Quiet
202.32										
.....	36.89	..	....	....	..	..	..	....	.....	In steamer chair
66.72	36.76	66	10.0	0.85	15	44	42	1.13	36.36	Quiet
72.33	36.71	66	10.5	0.82	14	53	33	1.18	38.01	Quiet
73.06	36.62	..	20.6	0.78	14	65	22	1.21	39.19	Fairly quiet
212.11										
.....	37.14	..	....	....	..	..	..	....	.....	Basal; flat in bed
89.22	36.94	49	21.0	0.84	18	46	36	1.14	36.14	
71.30	36.93	50	23.2	0.82	17	52	31	1.19	38.03	
160.52										
.....	37.10	..	....	....	..	..	..	....	.....	Sitting up with backrest at angle of about 30 deg.
70.46	37.05	53	1.9	0.85	16	44	40	1.06	33.58	
75.61	37.13	52	0.9	0.83	15	51	34	1.14	35.99	
146.07										
.....	37.03	..	....	....	..	..	..	....	.....	Basal; flat in bed
86.70	36.87	50	10.0	0.80	14	60	26	1.16	37.09	
65.32	36.94	47	0.6	0.81	14	56	30	1.14	36.26	
152.02										
.....	37.06	..	....	....	..	..	..	....	.....	Sitting up with backrest at angle of about 30 deg.
64.71	36.83	49	6.7	0.84	17	45	38	1.01	32.28	
67.15	36.86	46	3.7	0.86	16	40	44	1.05	33.67	
131.86										
.....	37.01	..	....	....	..	..	..	....	.....	Basal; flat in bed
66.94	36.95	54	3.5	0.88	15	34	51	1.12	35.99	
75.32	36.95	55	5.5	0.84	15	45	40	1.15	36.84	
142.26										

TABLE 5.—Clinical Data

Case No., Name and Date	Total Calories	Protein, Gm.	Fat, Gm.	Carb., Gm.	Food N	Urine N	Excreta N†	N Balance	NaCl Gm.	Urine Vol., c.c.	Body Weight, Kg.
Case 15, William A. Jan. 7- 8, 1915	2,753	94.1	126.0	29.15	15.05	13.86	15.37	−0.32	.....	1,255	62.38
Jan. 8- 9, 1915	3,075	112.2	152.9	291.4	17.95	13.82	15.62	+2.33	.....	1,230	.....
Jan. 9-10, 1915	3,207	97.4	131.9	385.5	15.58	14.54	16.06	−0.48	.....	1,530	.....
Jan. 25-26, 1915	1,756	72.0	99.0	131.6	11.52	9.52	10.67	+0.85	.....	1,232	63.44
Jan. 26-27, 1915	2,588	76.4	102.8	321.7	12.55	.....	.....	.....	.....	.....	.....
Jan. 27-28, 1915	2,063	58.3	87.1	247.4	9.32	10.30	11.23	−1.91	.....	1,135	63.00
Case 5, Charles L. Feb. 19-20, 1915	1,514	33.3	69.8	177.3	5.33	8.55	9.08	−3.75	.....	685	85.84
Case 8, Henry R. Feb. 26-27, 1915	1,035	18.2	33.1	158.8	2.91	7.12	7.41	- 4.50	.....	417	74.59
Case 3, Fred D. Feb. 15-16, 1915	820	31.6	39.3	79.0	5.06	12.61	13.12	−8.06	.....	913	49.75
Feb. 16-17, 1915	514	24.5	28.0	37.6	3.92	14.28	14.67	−10.75	.....	2,350	.....
Feb. 17-18, 1915	832	35.3	39.2	78.6	5.65	11.69	12.26	−6.61	26.95	4,800	.....
Feb. 18-19, 1915	1,155	34.4	48.5	137.4	5.50	7.90	8.45	−2.95	20.48	1,880	.....
Bartolo D. Mar. 11-12, 1915	2,836	85.9	147.7	246.9	13.74	6.28	7.65	+6.09	.....	1,220	.....
Mar. 12-13, 1915	2,922	100.8	131.5	313.7	16.13	5.32	6.96	+9.17	.....	1,960	43.78
Mar. 13-14, 1915	3,498	96.9	192.1	320.6	15.50	7.17	8.72	+6 78	.....	1,820	43.88
Mar. 14-15, 1915	2,983	91.8	157.6	278.2	14.69	6.89	8.36	+6.33	.....	1,700	43.33
Mar. 15 16, 1915	2,315	78.3	119.0	216.4	12.53	6.49	7.74	+4.79	.....	1,259	41.80
Morris S. Dec. 17-18, 1914	1,930	56.6	75.0	244.2	9.06	11.69	12.60	−3.54	.....	1,775 Cal. Spec.	61.21
Dec. 11-18, 1914	558 Protein meal	69.1	11.8	47.1	9.98	6.24 Cal. Spec.	.....	.....	.....	875	62.81
Case 9, Burrell P. Mar. 24-25, 1915	2,306	71.1	124.0	210.0	11.38	12.37	13.51	−2.13	.....	1,035	70.81
Case 11, William S. Feb. 10-11, 1915	1,726	40.0	95.3	164.9	6.40	10.61	11.25	- 4.85	.....	2,235	65.02
Feb. 11-12, 1915	2,444	59.9	117.4	269.7	9.60	.....	.....	.....	.....	1,695	.....
Case 7, Edward W. Feb. 24-25, 1915	1,423	44.2	58.8	169.6	7.07	7.26	7.98	−0.91	.....	1,254	54.35
Case 16, Theodore S. Jan. 28, 1914	2,021	88.4	94.8	189.5	14.1	.....	.....	.....	.....	800+	59.55
Jan. 29, 1914	2,034	96.3	87.3	201.7	15.4	.....	.....	.....	.....	1,025	60.10
Jan. 30, 1914	2,055	95.4	94.4	191.4	15.3	.....	.....	.....	.....	930	59.48

† Urine N + 10% of food N.

Patients with compensated cardiac lesions or with mild nephritis showed no increase in the metabolism. Of twelve patients with dyspnea, nine showed a distinct rise in metabolism, and in five of these the increase was from 25 to 50 per cent. above the average normal. Two out of the five gave evidence of marked acidosis in the low content of carbon dioxid in the alveolar air. In two others, whose metabolism was just as high, there was no significant depression of the alveolar carbon dioxid.

697 Huntington Avenue, Boston—477 First Avenue, New York.

REPORT OF CASES

Case 1.—Arthur V., aged 40, Italian, admitted Feb. 10, 1915, discharged March 3, 1915. Service of Dr. Nammack.

Diagnosis: Chronic nephritis, chronic myocarditis with decompensation.

Complaint: Dyspnea and cough.

Past History: Never sick before except for an attack of bronchitis three months ago. No history of venereal disease.

Present Illness: Has been "feeling poorly" for one month. For twelve days has had shortness of breath.

Physical Examination (February 12): The patient is a well built and fairly well developed man. Height 155 cm. Skin is slightly yellowish. Sclerae clear. He is dyspneic and orthopneic. There is a slight cyanotic tinge to his lips and ears. Respiration is rapid and shallow; rate 30. Pneumographic tracings show respiration to be periodic in type. Heart: Dulness extends from 16 cm. to the left of the midsternum in the fifth space to 5 cm. to the right in the third space. The action is regular. At the apex there is a weak first sound with a faint systolic murmur and a weak second sound. Gallop rhythm at the apex. Pulmonic second sound is louder than the aortic second sound. No murmurs at the base. Radial artery not palpable. Lungs: Slight dulness at extreme right base posteriorly. Large moist râles at both bases. Abdomen, negative. Liver: Dulness extends 3 cm. below the costal margin. Edge indistinctly felt. No edema.

Pulse: Varied in rate from 72 to 116 between February 10 and February 18.

Temperature: Between February 10 and February 18 varied between 97.8 and 101 F. except on February 13, when it reached 103 F. (rectal), February 16, when it was 102.2 F. (rectal), and February 17, when it was 102.4 F. (rectal).

Urine: February 10, specific gravity, 1.026; albumin, very faint trace. One hyaline cast.

February 14, specific gravity, 1.020; albumin, cloud. Few casts.

February 23, specific gravity, 1.020; albumin, faint trace. No casts.

Blood Pressure: February 15, systolic, 110 mm.; diastolic, 70 mm.

February 16, systolic, 120 mm.; diastolic, 75 mm.

February 24, systolic, 120 mm.; diastolic, 60 mm.

Phenolsulphonephthalein Test: February 15, first hour, 20 per cent.; second hour, 12 per cent.; total, 32 per cent.

February 27, first hour, 50 per cent.; second hour, 13 per cent.; total, 63 per cent.

March 2, 1915: Roentgenoscopy does not reveal evidence of aneurysm or dilatation of the aorta. Cardiac shadow is triangular in shape with enlargement of the right heart. Cardiophrenic angle is obtuse.

Medication: Patient was on a "soft special" diet, consisting chiefly of milk, cream, bread, butter and eggs. Strophanthin, 0.5 mg., intramuscularly, on February 10. Digitalis from February 13 to February 22, inclusive.

Diet Chart Summary

Date	Food Calories	Food N, Gm.	Urine Vol., C.c.	Urine N, Gm.
2/12/13	1,246	7.28	560	10.27

Alveolar Air (Plesch-Higgins method): February 12, 23.9 mm.; February 16, 30.8 mm.; February 27, 41.0 mm.

Electrocardiogram: February 26, "R" waves small in all leads, directed down in lead 3. "P" waves larger in all leads.

In the ten days following the observations in the calorimeter, the patient's condition showed little change. His dyspnea, though of only moderate grade while he was at rest, improved but little. Physical examination remained practically unchanged.

In calorimeter, Feb. 12, 1915, No. 189.

February 13, the dyspnea is somewhat less marked. The pulse is a little smaller and the heart action not quite so strong.

February 26, seems improved. Much less dyspneic. Pulse suggestive of a Corrigan.

Case 2.—Armon W., aged 33, pedler, born in Hungary, admitted Feb. 9, 1915, discharged Feb. 18, 1915. Service of Dr. Nammack.

Diagnosis: Mitral stenosis and insufficiency. Auricular fibrillation.

Complaint: Pain in heart and right side.

Past History: Was never sick up to six months ago. Has been in hospitals twice during last six months on account of dyspnea and swollen feet. No history of rheumatism or syphilis.

Present Illness: No improvement since discharged from Beth Israel Hospital.

Physical Examination (February 13): Patient is a fairly well built young man. Height 161 cm. Respiration, 28 per minute. Slight cyanosis. Heart dulness extends from 12 cm. to left of the midsternum in the fifth interspace to the right sternal border of the sternum. First sound at apex is loud and is followed by a rumbling systolic murmur. Second sound is loud and is followed by a rumbling diastolic murmur which extends through the short diastoles but is followed by a pause before the first sound in the longer diastoles. Both second sounds are normal at the base. Action absolutely irregular. Practically all the beats reach the wrist.

Temperature: Normal.

Pulse: From 156 to 72.

Respiration: From 26 to 28. During last three days it was from 20 to 24.

Medication: Special diet. Infusion of digitalis, every four hours from February 9 to 10.

Wassermann (Feb. 10, 1915): +++.

Blood Pressure (February 18): Systolic, 110; diastolic, 70.

Urine: February 10, specific gravity, 1.022; albumin, 0; no casts.

February 17, specific gravity, 1.030; albumin, faint cloud; no casts.

Alveolar Air (Plesch method): February 13, carbon dioxid tension 44.2 mm.

In calorimeter Feb. 13, 1915.

Case 3.—Fred D., aged 17, clerk, admitted Feb. 13, 1915, discharged March 19, 1915. Service of Dr. Nammack.

Diagnosis: Mitral stenosis and insufficiency.

Complaint: "Shortness of breath."

Past History: First attack of rheumatism at the age of 6 years. He made a complete recovery and was well until a second attack of rheumatism at 11 years of age. Since then he has been perfectly well up to the present illness.

Present Illness: Began three weeks ago with pain in the abdomen. He stopped work for one week but after that went back to work for two weeks. During the week before admission to the hospital he was troubled with marked shortness of breath. Edema of feet began on the day before admission. He has had a cough for three days.

Physical Examination (February 16): The patient is 157 cm. tall. He is slightly cyanotic and orthopneic. No clubbing of fingers. Heart: Apex impulse is in the fifth space 9 cm. to the left of the midsternal line. Cardiac dulness extends from 12 cm. to left of midsternum in the sixth space to 5 cm. to the right in the fourth space. Action regular. At the apex the first sound is followed by a blowing systolic murmur; the second sound is distant and followed by a long rumbling murmur which extends through diastole. The pulmonic second sound is accentuated. There is a loud systolic murmur in the fourth and fifth spaces just to the left of the sternum and transmitted to the right. The lungs are negative except for scattered râles and dulness at the extreme left base. Liver not felt. Abdomen negative. Slight edema of legs.

Urine: Specific gravity, 1.030; heavy cloud of albumin; many casts.

Temperature has ranged from 100 to 102 since admission.

Pulse has varied between 96 and 112; respirations from 24 to 32.

The patient was in the calorimeter, February 15, the day preceding the foregoing physical examination, and on February 23.

February 19: The patient is now almost completely compensated at rest. Respiration less rapid and less labored. Slight cyanosis persists. Heart dulness extends from 10 cm. to the left in the fifth space to 3.5 cm. to the right in the fourth space. Action regular. Sounds and murmurs are unchanged. He has been passing large quantities of water.

Date	Food Cal.	Food N.	Urine N.	Urine NaCl	Urine Vol., C.c.
2/15-16			12.61		913
2/16-17	518	3.92	14.28		2,430
2/17-18			11.69	26.95	4,800
2/18-19	1,139	4.90	7.90	20.48	1,880

February 24: Blood pressure: systolic, 95; diastolic, 70.

February 17-24, temperature varied between 98.4 and 99.8 (rectal).

February 20: Urine: Albumin negative, no casts.

The patient was on the Karrell diet and received digitalis from February 14 to February 17, inclusive.

February 24: Blood culture sterile. Wassermann negative.

March 13: Up and about.

Alveolar Carbon Dioxid (Plesch-Higgins method): February 15, average 27.7 mm.; February 16, average 33.7 mm.; February 18, average 36.7 mm.; February 23, average 37.2 mm.

Medication: Digitalin, 10 minims every four hous (8, 12, 4) the night before going into the calorimeter (Feb. 15, 1915). Also digitalin, 10 minims, every four hours (8, 2, 6) on the day of the calorimeter (Feb. 15, 1915).

No electrocardiogram.

Case 4.—Edward M., aged 37, chauffeur, born in the United States, admitted Feb. 15, 1915, discharged Feb. 27, 1915. Service of Dr. Coleman.

Diagnosis: Mitral insufficiency and auricular fibrillation.

Complaint: Dyspnea and edema of the legs.

Family History: Negative.

Past History: Had rheumatism in 1908. The attack lasted about one year, and affected all the joints of his limbs. He was in bed off and on. Four years ago he was refused life insurance. He has had dyspnea, palpitation, edema of the feet and vertigo for several years. During the last year these symptoms have been severe. This is his third admission to the hospital since last May. No history of venereal disease.

Present Illness: Legs have been more swollen during the last week. Dyspnea and cough are more severe, so he has returned to the hospital.

Physical Examination (Feb. 17, 1915): The patient is a large, well developed man. He is orthopneic and distinctly cyanotic, but his respiration is

slower and not so labored as it was yesterday. He coughs occasionally but raises little sputum. Heart: Dulness extends from 14 cm. to the left of the midsternum in the fifth space to 4 cm. to the right in the fourth space. Pulse 86, irregular in force and rhythm. No pulse deficit. At the apex the first sound is poor in quality, and is followed by a blowing systolic murmur which is transmitted to the left. No murmurs at the base. Pulmonic second sound is louder than the aortic. Radial artery not palpable. Lungs: Slight dulness at the left base posteriorly. Numerous sibilant and sonorous râles throughout the chest. Liver: Edge indistinctly made out 5 cm. below the costal margin in the right mammary line. No fluid in the abdomen. Slight edema of the back and legs.

Pulse, between February 16 and February 20, ranged from 56 to 108. It was 120 once, and 140 once.

Temperature reached 102 F. (rectal), February 16. From then to February 20 it was below 99.8 F. (rectal).

Respiration varied from 24 to 30 on the first three days in the hospital, and was subsequently 20 or less.

Blood Pressure: February 16, systolic, 120; diastolic, 85.

Urine: February 16, specific gravity, 1.025; trace of albumin; no casts.

Medication: Soft diet. Digitalis from February 16 to February 19, infusion of digitalis, 20 minims, the night before and on the day he was in the calorimeter.

Alveolar Air (Plesch method): February 16, carbon dioxid tension, 38.3 mm.

Electrocardiogram shows auricular fibrillation. "T" waves directed down in the second and third leads.

Patient regained compensation rapidly, and on February 24 was beginning to get up in a chair.

In calorimeter, Feb. 17, 1915.

Discharged, Feb. 27, 1915. General condition very good. Cyanosis much improved. Walks around without shortness of breath. Pulse still irregular.

Case 5.—Charles L., aged 54, laborer, born in the United States, admitted February 16, 1915, discharged Feb. 24, 1915. Service of Dr. Lambert.

Diagnosis: Chronic nephritis with hypertension. Cardiac hypertrophy with aortic insufficiency and mitral insufficiency. Emphysema.

Complaint: Shortness of breath.

Family History: Negative.

Past History: Three years ago he was sick for nine weeks with rheumatism. He had erysipelas following a fracture of the skull six years ago. He drinks a considerable amount of beer. There is no history of syphilis.

Present Illness: He has noticed dyspnea for about a month when he went upstairs. For two weeks this has been much worse and he has been unable to sleep at night.

Physical Examination (February 19): The patient is a rather large, strong man. His skin has slight yellowish tinge. Lips and mucous membranes are of fair color. There is no definite cyanosis. Respiration is quiet but somewhat rapid. Respiration is periodic in type, but without intervals of complete apnea. The chest is large, almost barrel-shaped. Heart: Dulness extends from 14 cm. in the fifth space to the left of the midsternum to the right sternal margin. No area of absolute cardiac dulness. Action regular. At the apex the first sound is rather faint and it is followed by a blowing systolic murmur. The second sound at the apex is also faint; it is followed by a blowing diastolic murmur. Both systolic and diastolic murmurs are well heard in the axilla and over the precordium. They are also audible in the first and second spaces to the right of the sternum. The murmurs are loudest in the first space to the right and in the second space to the left of the sternum. The pulse is of good size, high tension, and distinctly collapsing in type. Artery wall not palpable. Lungs: Emphysematous. Scattered râles in both sides of back. Fairly frequent cough, but little expectoration. Dulness with absent breath sounds at extreme right base posteriorly. Abdomen negative except for slight tenderness in region of the liver. Liver not felt. No edema.

Temperature: Varied between 98 and 100 F. (rectal).

Pulse: Varied between 64 and 100.

Respiration: Ran between 28 and 36 on the first two days—later between 20 and 28.

Wassermann Reaction: Negative.

Blood Pressure: February 17, systolic, 180; diastolic, 90.

Phenolsulphonephthalein Test: February 20, first hour, 10 per cent.; second hour, 20 per cent.; total, 30 per cent.

Urine: February 16, specific gravity, 1.020; albumin, heavy cloud; many casts.

February 21, specific gravity, 1.018; albumin, strong trace; many casts.

Summary of Diet Chart

Date	Food Cal.	Food N.	Urine Vol., C.c.	Urine N.	Urine NaCl
2/19-20	1,524	5.82	685	8.55	12.17

Medication: Special diet. Restricted fluids. Infusion of digitalis every four hours from February 18 to February 20. Infusion of digitalis just before going into calorimeter.

Alveolar Air (Plesch method): February 19, carbon dioxid tension, 39.4 mm. at 3:30 p. m.

In calorimeter, Feb. 19, 1915.

Case 6.—Annie T., aged 14, born in the United States, admitted Jan. 14, 1915, discharged March 25, 1915. Service of Dr. Lambert.

Diagnosis: Congenital heart disease. Open ventricular septum. Dextrocardia.

Complaint: Heart trouble, headache and trembling.

Family History: Negative.

Past History: Negative except for the dyspnea associated with her cardiac condition.

Present Illness: Comes to hospital on account of a severe attack of headache, with palpitation of the heart, and stomach ache. Has had similar attacks before.

Physical Examination: Height 137 cm. The patient is a small, rather underdeveloped girl, dull mentally. She lies flat on her back breathing quietly but slightly rapidly. There is a high degree of cyanosis of lips, tongue, nose, hands and feet. There is marked clubbing of the fingers and toes. The chest is asymmetrical. Right side more prominent than left. Heart: Apex impulse is in the fifth space 9 cm. to the right of the midsternal line. The dulness extends from 11 cm. to the right in the fifth space to 4 cm. to the left of the midsternum in the fourth space. No thrills are felt. At the apex, just below and outside the right nipple, the first sound is scarcely audible, and there is a loud blowing systolic murmur. The second sound is weak. There is a loud systolic murmur heard all over the precordium and to the left of the sternum. Its maximum intensity is in the fifth space just to the right of the sternum. There is a loud, low pitched systolic murmur in the second space just to the left of the sternum, and also in the second space to the right of the sternum. Lungs: Negative on auscultation and percussion. Abdomen, liver and spleen negative. Skin harsh and dry.

Roentgenoscopy reveals transposition of heart and colon. Stomach and liver are in normal position.

Temperature: Ranges between 98.4 and 101 F. (rectal).

Pulse: Usually varies between 86 and 108.

Respiration: Now from 20 to 24.

Blood Pressure: January 27, systolic, 95 mm.

Urine: January 15, specific gravity, 1.025; albumin, cloud; granular casts.

Alveolar Air (Plesch method): February 18, carbon dioxid tension, 25.2 mm. at 4 p. m.

Blood: Jan. 28, 1915, leukocytes, 14,000; polymorphonuclears, 63; transitionals, 1; lymphocytes, 28; large mononuclears, 8; mast cells, 0.

Feb. 9, 1915, leukocytes, 15,200; polymorphonuclears, 56; transitionals, 4; lymphocytes, 28; large mononuclears, 7; mast cells, 5.

Electrocardiogram, Jan. 16, 1915, shows an inverted "T" wave in the first lead; very large "P" and "T" waves in the second lead, and very large "P" and "T" waves in the last lead, with a splitting of the "T" waves.

Electrocardiogram: Jan. 19, 1915, right and left arm terminals were normal. Shows right heart preponderance; inverted "P" and very large "T" waves in Lead 1; "P-R" interval prolonged.

In calorimeter, Feb. 20, 1915.

Case 7.—Edward W., aged 37, born in the United States, bath attendant, admitted Feb. 22, 1915, discharged March 7, 1915. Service of Dr. Meara.

Diagnosis: Chronic interstitial nephritis. Cardiac dilatation.

Complaint: Shortness of breath; swelling of feet.

Past History: Has had frequent attacks of sore throat. Syphilis twelve years ago. Has been a heavy drinker during the last three months.

Present Illness: Five days before admission he began to be troubled with palpitation and dyspnea on exertion. Dyspnea has been much worse at night. Edema of feet for the last few days.

Physical Examination (February 24): The patient is a fairly well developed young man. His lips, ears and finger tips are slightly dusky. Definite exophthalmos. Thyroid not enlarged. Respiration is periodic, but without intervals of complete apnea. Breath urinous. Orthopnea marked. Patient says he is breathing much more easily than during the night. Heart: Dulness extends from 11 cm. to the left of the midsternum in the fifth space to 3.5 cm. to the right of the midsternum in the fourth space. At the apex the first sound is loud, followed by a soft, blowing systolic murmur and a ringing second sound. Aortic second is ringing but not accentuated. Gallop rhythm is heard all over the precordium, most marked just below the left nipple. Pulse is regular; high tension. Wall of radial artery is easily palpable. Vessels tortuous. Lungs: Negative except for scattered râles, which are most numerous at the left base. Abdomen negative. Liver negative. Very slight edema of the dependent parts of the thighs.

Pulse: From February 22 to February 25, has averaged from 86 to 116 per minute.

Respirations: From February 22 to February 25, have averaged from 20 to 32 per minute.

Temperature: From February 22 to February 25, has varied from 98.4 to 99.8 F. (rectal).

Blood Pressure: February 23, systolic, 190; diastolic, 100 mm.

Urine: February 23, specific gravity, 1.018; albumin, + + +; no casts seen.

Medication: Soft diet. Tincture of digitalis, 15 minims, every four hours from February 22 to 28.

Summary of Diet Chart

	Food		Urine	
Date	Cal.	Food N.	Vol., C.c.	Urine N.
2/24-25	1,226	3.36	1,254	7.26

Alveolar Air (Plesch method): February 24, carbon dioxid tension, 38.9 mm.

Wassermann, Feb. 28, 1915, positive, 17 units.

Alkali Tolerance Test: After 20 gm. sodium bicarbonate, given in 5 gm. doses every hour, the urine became neutral. After 25 gm. it was still neutral. Not tested later.

Phenolsulphonephthalein Test: February 27, first hour, 6 per cent.; second hour, 4 per cent.; total, 10 per cent.

February 27: The patient has Cheyne-Stokes respiration—periods of apnea and periods of intense dyspnea. He is very uncomfortable with his breathlessness. His condition appears to be much worse.

In calorimeter, Feb. 24, 1915.

March 7, 1915: Patient has improved very little. Fairly comfortable during the day, but each night suffers from shortness of breath and great restlessness. Heart action is rapid, and there is a gallop rhythm in spite of digitalis. Respiration is of Cheyne-Stokes type. Left hospital against advice in a serious condition. Died April 17, 1915.

Case 8.—Henry R., aged 40, born in the United States, waiter, admitted to hospital, Jan. 22, 1915, died March 20, 1915. Necropsy not obtained. Service of Dr. Nammack.

Diagnosis: Chronic myocarditis. Emphysema. Chronic nephritis (?).

Complaint: Shortness of breath.

Past History: Syphilis three years ago. Was in Bellevue Hospital in May, 1914, with lobar pneumonia. Has been in hospital since then with diagnosis of chronic myocarditis the first time, and chronic cardiac valvular disease the second time. Drinks two or three whiskies a day.

Present Illness: Comes into the hospital again because of increase of dyspnea since catching cold. On admission the clinical picture was that of an acutely decompensated heart. February 6, he began to run an irregular temperature, reaching sometimes 103, rectal. The diagnosis of bronchopneumonia was considered. February 21, the temperature fell to normal. Since then the highest temperature has been 101, rectal. General condition has not improved essentially.

Physical Examination (February 26): The patient is a big strong negro 153 cm. tall. Respiration is very rapid and shallow; rate, 40. There is orthopnea. Tongue and conjunctiva are rather pale. Eyes are prominent. Chest is very large. Heart: Dulness extends from 12.5 cm. to the left of the midsternum in the fifth space to 3 cm. to the right in the fourth space. The action is regular and rapid. Sounds are of fair quality. No murmurs are heard. There is a well marked protodiastolic gallop rhythm, heard best just below and outside the left nipple. Aortic second sound is slightly accentuated and ringing. Pulse is of fair quality; rate, 116 per minute. Artery wall not palpable. Lungs: Marked emphysema. Slight dulness at extreme right base posteriorly. A few scattered râles throughout both lungs. Many moist râles at the right base behind. Abdomen, negative. Liver: Edge easily felt about 3 cm. below the costal margin in the right nipple line. Slight tenderness over the liver. Very slight edema of the feet and lower legs.

Urine: Clear, amber, 1.022 specific gravity, acid, heavy cloud of albumin, many hyaline and coarsely granular casts, many leukocytes.

Blood Pressure: February 18, systolic, 138; diastolic, 105.

February 27, systolic, 160; diastolic, 120.

Phenolsulphonephthalein: Feb. 27, 1915, first hour, 30 per cent.; second hour, 18 per cent.; total, 48 per cent.

Wassermann, January 30, double positive, 12 units.

Alveolar Air (Plesch-Higgins method): February 25, carbon dioxid tension, 41.1 mm. at 5 p. m. February 26, carbon dioxid tension, 39.9 mm. at 4:30 p. m.

Medication: Soft diet. Morphin. Infusion of digitalis. Tincture digitalis. Codein ¼ grain, the night before and the morning before going into calorimeter.

Temperature: January 22 to Jan. 28, 1915, 99 to 101. January 28 to Feb. 1, 1915, 99. February 2 to Feb. 7, 1915, rose to 103.5 once. February 8 to Feb. 12, 1915, 100 to 101.5. February 12 to Feb. 16, 1915, 100 to 104. Remainder of time, 99 to 101.

In calorimeter, Feb. 26, 1915.

Case 9.—Burrell P., aged 41, laborer, admitted March 18, 1915, discharged April 5, 1915. Service of Dr. Nammack.

Diagnoses: Aortic regurgitation and stenosis. Mitral regurgitation. Tricuspid regurgitation. Aneurysmal dilatation of the aorta.

Chief Complaint: Shortness of breath.

Past History: Measles and whooping cough as child. Pneumonia twenty years ago.

Present Illness: Duration for past year. Ten weeks ago found that he could not work properly on account of shortness of breath. Has had hoarseness and sore throat. Nocturia rather frequent. Occasional headaches. Marked dyspnea, especially after work. Has had no swelling of ankles or legs at any time. Coughs frequently and has marked night sweats.

Physical Examination (March 23, 1915): Patient is a dark negro of muscular development. Is 169 cm. (5 feet 7 inches) tall. Orthopneic and dyspneic, breathing 26 to the minute. Not prostrated nor in much distress. An occasional unproductive cough. Heart: Apex beat in sixth space, 15 cm. to the left. Action is regular, not rapid; forceful. At the apex there is a blowing systolic murmur transmitted to the left, and a waterfall, diminuendo diastolic murmur heard with maximum intensity to the left of the sternum, but audible over the whole precordium. In the third left space there is a short presystolic murmur (Flint?). Over the aortic region there is a harsh systolic and a soft diastolic murmur. Pulse: Large excursion, quick rise and fall. Artery wall moderately thickened. Lungs: No dulness; many sibilant and sonorous râles. Cervical, axillary, epitrochlear, inguinal glands considerably enlarged.

March 19, 1915: Electrocardiogram shows a large "P" wave and the "T" wave is directed upward in each lead. There is marked left sided preponderance.

April 1, 1915: Some dyspnea. Complains of precordial pain. Heart not much changed.

Urine: Negative.

Blood: No data.

Temperature ran to 101.5 F., March 18, 1915; below 100 F. the rest of the time.

Pulse: March 18, 1915, from 104 to 112; March 19, 1915, from 70 to 80.

Respiration: March 18, 1915, from 20 to 32.

In the calorimeter, March 24, 1915.

March 18, 1915: Pupils unequal. React sluggishly. Aortic arch is dilated and heart is greatly enlarged down and to the left, also to the right of the midsternal line. Systolic thrill palpable over the aortic area. Apical impulse is forceful. Systolic and diastolic murmur is heard at the apex. Aortic second sound is accentuated. A systolic murmur is heard over the tricuspid area. There is an extracardiac sound heard which appears to be a pericardial rub. The pulse is of a typical Corrigan type.

March 22, 1915: Condition improved. Rhythm regular. Rate slow. Pericardial scratch persists. Seems much better compensated.

Medication: Digitalin, 15 minims, every four hours, the day before going into the calorimeter. Also ¼ grain codein, the night before going into the calorimeter.

Case 10.—August F., aged 62, tailor, married, admitted April 26, 1915, died May 20, 1915.

Diagnosis: Chronic interstitial nephritis and auricular fibrillation.

Complaint: Shortness of breath. Swelling of feet. Pain in chest.

Past History: There is a family history of cardiac disease. He was told that he had albumin in the urine many years ago. He had pneumonia long ago. Has had no rheumatism. Three months ago fluid was removed from his chest.

Present Illness: Began three years ago with a feeling of fatigue and shortness of breath. He has had remissions ever since. Also occasional headaches and night sweats. He feels very weak.

Physical Examination: The patient is 159 cm. tall. He is very orthopneic and in considerable distress. His lips are dry and cyanotic. Teeth are bad.

There are many râles over both bases of the lungs. Heart: Right border 3 cm. from the midsternal line. Upper border at the third rib. Left border 14 cm. and the apex 13 cm. from the midsternal line. There is a faint systolic blow heard over the apex. The sounds are of poor muscular quality. There is a harsh systolic murmur heard over the aortic area. The pulse is somewhat irregular. Walls palpable.

April 27: Pulse slower after strophanthin and digitalis.

April 29: A rough, hard systolic murmur is heard over the base of the heart, loudest in the third left space. The second sound is also loudest in this site. There is a moderate amount of fluid in the abdomen. Edema of the extremities.

May 1: Dulness at both bases posteriorly. Breath sounds diminished in intensity at the bases, where one hears an occasional râle. The cardiac impulse is less pronounced than on admission. The heart is still much dilated. There is a rough blow at the mitral area. The aortic second sound is slightly prolonged. The heart impulse is in the fifth space, 12 cm. to the left of the midline. The left limit of dulness is in the sixth space, 12.5 cm. to the left of the midline. Right limit of dulness is in the fourth space, 4 cm. to the right of the midline. There is a systolic murmur of maximum intensity to the right of the sternum. The patient has very scant beard. Pubic hair of female type. The patient is very orthopneic · distir ctly dyspneic and shows marked Cheyne-Stokes breathing when asleep or quiet. He is slightly cyanotic. There is distinct edema of the flanks and legs. The breath is slightly urinous.

Urine: Cloudy, amber colored, specific gravity, 1.010, trace of albumin, hyaline and granular casts, leukocytes, erythrocytes.

Blood Pressure: Systolic, 170; diastolic, 110 (?), May 1, 1915.

Blood: Leukocytes, 15,600; polymorphonuclears, 68 per cent.; transitionals, 3 per cent.; lymphocytes, 25 per cent.; large mononuclears, 4 per cent.

Temperature: April 27 to May 12, from normal to 100; May 13 to May 19, 103.

Respiration: During high temperature, from 24 to 32.

Pulse: During high temperature, from 104 to 120.

Electrocardiogram: May 3, shows auricular fibrillation and left hypertrophy.

Phenolsulphonephthalein Test: May 8, first hour, 13 per cent.; second hour, 11 per cent.; total, 24 per cent.

The patient grew more and more orthopneic and dyspneic until death. Breath became more urinous.

Case 11.—William S., aged 48, longshoreman, admitted Dec. 22, 1914, discharged March 1, 1915. Service of Dr. Coleman.

Diagnosis: Adherent pericardium and auricular fibrillation.

Complaint: Shortness of breath. Pain in lumbar region.

Past History: Healthy until 1913, when he had pneumonia and was in Ward B2 of the Bellevue Hospital. After discharge he was weak and dyspneic for two months and was unable to work. Since then he has had a productive cough. He has lost weight and has had hemoptysis. There is a positive history of syphilis and gonorrhea.

Present Illness: Dec. 22, 1914, while unloading heavy lumber, he became suddenly short of breath. He rested but obtained no relief.

Physical Examination: The patient is 171 cm. tall, a moderately well nourished man, propped up in bed, markedly dyspneic and somewhat cyanotic. Pupils are sluggish. He is breathing rapidly and shallowly. There is diffuse systolic impulse over a broad area at the apex. The area of absolute cardiac dulness is very much enlarged. The sounds are of poor quality. There are no murmurs. The abdomen is distended and somewhat tender. The liver is felt at the umbilicus. Heart: Right border is 10 cm. to the right of the midline; left border, 14 cm. to the left of the midline. A triangular area of dulness.

Wassermann: Anticomplementary.

Jan. 2, 1915: General condition much improved. Broadbent's sign present.

Jan. 27, 1915: Patient sat up for two hours without any ill effect.

Feb. 3, 1915: Three days ago the patient developed shortness of breath; precordial pain; edema of the extremities.

Feb. 10, 1915: Dyspnea less marked. Cyanosis persists. Heart action very irregular, sounds faint, no distinct murmurs. Regurgitant wave in the jugulars. Few moist râles at bases.

Feb. 28, 1915: Distention of abdomen relieved by catharsis. Dyspnea continues. Heart irregular. Condition improved slightly.

Urine: Dec. 23, 1914, clear, pale amber, specific gravity 1.020, acid, faint trace of albumin, few hyaline casts.

Blood: Dec. 24, 1914, leukocytes, 4,800; polymorphonuclears, 73 per cent.; transitionals, 5 per cent.; lymphocytes, 12 per cent.; large mononuclears, 8 per cent.; eosinophils, 1 per cent.

Temperature: December 23 to December 25, from 101 to 103 F. December 26 to Feb. 28, 1915, from normal to 99 F.

Pulse: In the beginning from 100 to 146; later, from 60 to 80; then from 80 to 95.

Respiration: In the beginning, from 28 to 36; later, from 24 to 28.

Blood Pressure: Dec. 26, 1914, systolic, 110; diastolic, 80 (?).

Electrocardiogram: December 28, auricular fibrillation; "T" waves directed down in all leads.

Roentgenoscopy: December 30, moderate enlargement to the right and left; marked irregularity in the outline of the right diaphragm suggesting extensive adhesions.

In calorimeter, Feb. 10, 1915.

Case 12.—George M., aged 56, saloonkeeper, watchman, porter, admitted Jan. 19, 1914, discharged April 29, 1914. Service of Dr. Meara.

Diagnosis: Chronic interstitial nephritis and cardiac hypertrophy.

Complaint: Shortness of breath. Swelling of the feet.

Past History: Alcoholic. Had measles when a child. Gonorrhea thirty-four years ago.

Present Illness: In December, 1911, he first noticed shortness of breath on exertion and swelling of feet after work. Had to stop work about the 10th of June, 1911, because of the shortness of breath and edema of feet. His abdomen then began to increase in size and he became yellowish in color. His scrotum and penis began to swell. Frequent micturition. Oct. 23, 1912, he was taken with shortness of breath again, cough and swelling of the legs. Aug. 5, 1913, his legs began to swell, and he became very dyspneic on walking. His sputum became bloody. He could not lie down in bed on account of dyspnea. His abdomen increased in size.

Physical Examination (Jan. 19, 1914): The patient is a well nourished man propped up in bed showing considerable dyspnea. His face is flushed and somewhat edematous. Chest symmetrical and emphysematous. Sibilant and sonorous râles anteriorly and posteriorly. Heart: Right border 7 cm. to the right; left border 13 cm. to the left; cardiac impulse 12.5 cm. from the midsternal line. It extends to the third rib above. The sounds at the apex are of poor muscular quality. There are extrasystoles, some of which are not felt at the wrist. At the base the sounds are distant. No murmurs can be definitely made out. The pulse is irregular in force and rhythm. The vessel walls are slightly thickened. Liver dulness extends 2 cm. below the costal margin. Extremities edematous.

Jan. 22, 1914: Left lung shows dulness to flatness from the angle of the scapular to the base with a pleuritic rub. Heart: Left border 13 cm. from the midsternal line in the fourth-fifth interspace; right border 7 cm. from the midsternal line in the third-fourth interspace. Extends to third rib above.

Feb. 23, 1914: Doing well. No edema. Heart regular. Patient has a pulsus alternans.

March 14, 1914: Looks very well. On sodium chlorid has incomplete elimination with formation of an edema and increased blood pressure. On potassium chlorid the elimination is complete, associated with diuresis and fall of blood pressure.

April 28, 1914: General condition excellent. Heart as noticed above. Discharged.

Urine: Nov. 10, 1912, cloudy, amber, specific gravity 1.022, acid, faint trace of albumin, finely granular casts, leukocytes +, erythrocytes +.

Blood: Dec. 6, 1912, leukocytes, 11,000; polymorphonuclears, 73 per cent.; transitionals, 7 per cent.; lymphocytes, 15 per cent.; large mononuclears, 8 per cent.; hemoglobin, 90 per cent.; reds, 4,504,000.

Blood Pressure: March 24, 1914, systolic, 195; diastolic, 115. April 4, 1914, systolic, 160; diastolic, 102.

Pulse: March 24, 1914, from 72 to 90; April 4, 1914, from 72 to 80.

Respiration: March 24, 1914, from 18 to 24; April 4, 1914, from 20 to 24.

Temperature: March 24, 1914, subnormal; April 4, 1914, subnormal.

Wassermann: Dec. 8, 1913, positive.

Phenolsulphonephthalein: Jan. 27, 1914, 55 per cent. in two hours.

Case 13.—Marcus R., aged 51, Hebrew, tinsmith, admitted March 10, 1913, discharged April 12, 1913. Service of Dr. Thompson.

Diagnosis: Chronic interstitial nephritis, arteriosclerosis, mitral insufficiency.

Past History: He had malaria at the age of 17 to 20 years. Had pneumonia in 1877. He is a moderate user of alcohol; occasionally took whisky before breakfast.

Present Illness: In January, 1912, his legs began to swell. Since then he has been short of breath and has not been able to walk. He has been very thirsty and gets up once or twice at night to pass water. Three weeks ago he caught cold.

Physical Examination: The patient is of medium stature and heavy build. He is slightly dyspneic. The apex is in the fifth space, 14 cm. from the midline. The sounds are booming. There is a loud systolic murmur at the apex. The aortic second sound is very much accentuated. The artery wall is very thick, and there is a question of calcification. Tension is high. Pulse is regular. Many crackling and moist râles over the lungs. Liver edge is felt one hand's breadth below the costal margin. The surface is hard and nodular. There is shifting fluid in the flanks.

Urine: March 10, from 600 to 1,400 c.c.

Blood Pressure: March 10, systolic, from 300 to 320; diastolic, from 140 to 180. March 16-31, systolic, 300 to 310; diastolic, 115 to 150. April 1-9, systolic, 300 to 320; diastolic, 150 to 170.

Temperature: March 10, from 98 to 100 F. March 16-31, normal. April 1-9, normal.

Pulse: March 10, from 88 to 100. March 16-31, 72 to 80. April 1-9, 78 to 84.

Respiration: March 10, from 20 to 30. March 16-31, 18 to 20. April 1-9, 18 to 20.

Weight: March 10, 149½ pounds. March 16-31, from 140 to 137 pounds.

Case 14.—David K., aged 54, architect in reduced circumstances, admitted Feb. 21, 1913, discharged March 26, 1913. Service of Dr. Hartwell.

Diagnosis: Chronic interstitial nephritis. Arteriosclerosis. Inguinal hernia.

Past History: Three years previous to admission he noticed a small lump in his left groin. There was little discomfort until two years later when it became painful. Is very alcoholic.

March 21, 1913: Four weeks ago the patient was operated on for inguinal hernia. He now seems absolutely normal. He was out on a pass yesterday and returned at 7 p. m. For breakfast he had a cup of coffee without sugar or milk.

March 26, 1913: Heart: apex neither visible nor palpable. Left limit of dulness in the fifth space, 12.5 cm. to the left of the midline. Over the aortic area there is a rough systolic impurity of the first sound. The second aortic sound is loud and ringing. There is no enlargement to the right of the sternum. The radials are palpable.

March 26, 1913: Patient discharged.

Urine: Trace albumin.

Blood Pressure: March 26, systolic, 195; diastolic, 110.

Case 15.—William A., aged 24, laborer, admitted Dec. 28, 1914, discharged Jan. 30, 1915. Service of Dr. Coleman.

Diagnosis: Aortic regurgitation.

Complaint: Pain in right side of chest. Difficulty of breathing when lying down.

Past History: Has had measles, pneumonia and rheumatism. Has had gonorrhea. Tonsils have given him trouble. Tonsils are enlarged.

Present Illness: Dec. 25, 1914, he was taken with a very sharp pain in his side. The following night he could not lie down. He felt his heart beating. He now feels weak and coughs a good deal.

Physical Examination: The patient is a well developed and well nourished young man 180 cm. tall. His tonsils are swollen and congested. The cardiac impulse is seen in a diffuse area around the nipple and is forcible. The upper border is in the third interspace; right border 4 cm. from the midsternal line; left border 13 cm. from the midsternal line. There is a Flint murmur at the apex, and also a diastolic murmur. Corrigan pulse.

January 11, 1915: Lungs are normal. Patient is comfortable except for a slight cough. The diastolic and Flint murmurs still continued. There is a short systolic murmur at the apex.

January 15: There is a blowing systolic murmur at the aortic region, transmitted along the vessels of the neck and arm.

January 26: The patient has been in a chair all day without fatigue. He was examined upright in the chair. The cardiac impulse was forceful, maximum in the fifth space. The left limit of dulness in the fifth space, 13.5 cm. from the midline, in the fourth space 11.5 cm. from the midline; right limit of dulness at the sternal margin. In the aortic region there is a systolic murmur transmitted upward and a blowing diastolic murmur transmitted downward. At the apex there is a short systolic murmur and a rumbling murmur in diastole. Pulse of Corrigan type.

Blood Pressure: Systolic 140.

Urine: Clear, amber, specific gravity 1.030.

Temperature: Dec. 31, 1914, to Jan. 2, 1915, from 99 to 101 F. Jan. 6, 1915, varied slightly around the normal.

Respiration: From 18 to 20.

Pulse: From 65 to 80.

Electrocardiogram: "T" waves directed downward in the second and third leads. In the calorimeter, Jan. 25 and 27, 1915.

Case 16.—Theodore S., aged 32, coachman, single, admitted Jan. 17, 1914, discharged Feb. 22, 1914.

Diagnosis: Chronic cardiac valvular disease. Cardiac hypertrophy and dilatation.

Past History: He had pneumonia at the age of 6 years. In 1906 he had typhoid fever. He has had no rheumatism. At 8 years of age he was operated on for some abdominal condition. He was a moderate user of beer, but for the last two or three years he has used none. He stopped working one year ago. In Sweden he did rough carpenter work one year. Last year he was a driver.

Present Illness: For four or five years he has been short of breath, especially on exertion. At times he has had a pain in his left side. For one month he has had a short, sharp, hacking cough. He sleeps well. He was obliged to take an

easy job three years ago, as the doctor said he had heart trouble. Eight months ago he could carry a trunk upstairs. For two weeks he has been confined to the house.

Physical Examination: The patient is of medium build, 169 cm. tall, a well developed and well nourished man. Arteries are palpable. Sibilant râles at both bases.

Jan. 19, 1914: Patient is quite comfortable, not dyspneic, slight cyanosis of the lips.

January 26: Condition excellent. Slight cough, no dyspnea, no orthopnea. Sat up in chair without fatigue. Apex beat in the fifth space, 12 cm. from the midline; left limit of dulness in the fifth space 14.5 cm. from the midline, in the fourth space 12.5 cm. from the midline; right limit of dulness in the third space 3 cm. from the midline, in the fourth space 4 cm. from the midline. Heart action very slow, heavy, irregular in force and rate. Tracings show absence of the "A' wave, typical auricular fibrillation. At the apex the first sound is sharp and short. The second sound is faint. There is a loud, rough, rumbling murmur starting almost immediately after the second sound and diminishing in intensity during diastole, lasting throughout the short diastolic pauses, but stopping before the end of the long diastoles. At the base of the heart the pulmonic second sound is very much accentuated. The radial pulse corresponds with the apex impulse. The beats vary in size. Wall not palpable. There are a few sibilant and sonorous sounds in the lungs. No edema. Mucous membranes are deep red and slightly cyanotic.

February 10: The patient is up and about. He can walk up one and a half flights of steps.

February 11: The patient was given 1/120 grain atrophin, repeated after twenty-one minutes. Five minutes after the second dose the pulse rate increased from 48 to 55; the apex rate increased up to 96, and there was a large pulse deficit. At the apex the rate became almost regular, but not so regular in force. Throt dry, pupils dilated. The patient felt bad the next day, "As if he had been on a debauch."

February 15: The patient is sitting in a chair. Pulse 49; blood pressure, large beats, systolic, 145; diastolic, 85. After climbing stairs, pulse, 46, diastolic blood pressure, 150; systolic, 85.

February 21: Sounds as before. Wassermann negative.

Temperature: January 17-27, from 98 to 100 F. From January 28 on, the temperature was normal.

Roentgenogram of heart:

	Upright	Horizontal
Left	11.3	12.85
Right	8.35	7.8
	19.65	20.65

No medication.

The patient caught cold at home and was readmitted, March 4, 1914, with bronchopneumonia. Heart sounds the same. Discharged March 27, 1914.

CLINICAL CALORIMETRY

SEVENTEENTH PAPER

METABOLISM AND TREATMENT IN DIABETES*

FREDERICK M. ALLEN, M.D., AND EUGENE F. DU BOIS, M.D.
NEW YORK

The experiments here to be described concern two patients with moderate diabetes treated by the oatmeal method in the metabolism ward of the Russell Sage Institute of Pathology and four Rockefeller Hospital patients with more severe diabetes transferred to Bellevue Hospital for study in the respiration calorimeter during various stages of the fasting treatment. Only very brief mention is possible of the literature[1] concerning the subjects touched upon in the experiments, namely, (1) the oatmeal and fasting treatment, (2) the dextrose-nitrogen ratio, (3) the respiratory quotient under certain conditions, and (4) the total metabolism in diabetes.

1. According to literature previously reviewed,[2] the von Noorden school no longer holds that oatmeal stands entirely alone in respect to the capability of utilization by diabetic patients, but nevertheless maintains that for some unknown reason it is superior to other forms of carbohydrate. On the other hand, Blum[3] and a series of later authors have been able to observe no difference in the clinical effects of oatmeal and other carbohydrates. Also von Noorden has claimed that cases of the worst type are the ones that do best on oatmeal, whereas in mild cases the method often fails. The opposing authors found that oatmeal, like other carbohydrates, was tolerated better in mild cases and worse in severe cases. Furthermore, even in the seemingly favorable cases where the carbohydrate balance is strongly positive, respiration experiments have usually shown little or no combus-

* Submitted for publication March 22, 1916.

* From the Russell Sage Institute of Pathology in affiliation with the Second Medical Division of Bellevue Hospital, New York.

1. A fuller review by one of the authors (F. M. A.) is to be published elsewhere.

2. Allen, Frederick M.: Studies Concerning Glycosuria and Diabetes, Harvard University Press, Cambridge, Mass., 1913.

3. Blum, L.: Les Hydrates de Carbone dans le Traitement du Diabete Sucré, Semaine Médicale, 1911, xxxi, 313; Ueber Weizenmehlkuren bei Diabetes mellitus, Beitrag zur Theorie der Verwendung der Kohlehydrate in der Therapie der Zuckerkrankheit, München. med. Wchnschr., 1911, lviii, 1433; Die Diät bei Diabetes gravis, Med. Klin., 1913, p. 702.

tion of carbohydrate. Thus Benedict and Joslin[4] concluded that the carbohydrate ingested produced no material effect upon the metabolism; and Joslin[5] shows the failure of either oatmeal or potato to raise the respiratory quotient, notwithstanding positive carbohydrate balances as high as 100 gm. Falta[6] states, without giving details, that a diabetic patient taking 400 gm. oatmeal daily without glycosuria showed no rise in the respiratory quotient on the first or second days, but on the third day a marked rise in the quotient occurred. Normal persons showed the usual prompt rise in the quotient; but when subjected to the customary program of the "oat cure," namely, first a period of carbohydrate-free diet, then the customary fasting or vegetable-day, then a period of 400 gm. oatmeal daily, a normal person showed the same behavior as the diabetic, in that the quotient rose only on the third day. The reason was believed to be that the organism, impoverished in carbohydrate, first stored the ingested starch as glycogen without burning any considerable quantity. The records of Rolly[7] and Roth[8] concerning the administration of different carbohydrates to diabetics show no appreciable changes in the quotients during the series of successive days in their experiments. Joslin[5] pointed out that the respiratory quotient of Benedict's fasting man rose promptly on taking mixed diet at the end of a thirty-one-day fast. Confirmation is necessary before it can be accepted that either a diabetic or a normal subject will store the carbohydrate of 400 gm. oatmeal for two days, and then suddenly show active combustion on the third day. Any such change in the respiratory quotient of a diabetic patient would more probably indicate an improvement in the power of carbohydrate combustion.

Von Noorden and all other writers admit that many cases of diabetes are so severe that neither the glycosuria nor the acidosis is cleared up by the oatmeal treatment. The method recently introduced,[9]

4. Benedict, F. G., and Joslin, E. P.: Metabolism in Diabetes Mellitus, Carnegie Institution of Washington, 1910, Pub. No. 136, pp. 203, 215; A Study of Metabolism in Severe Diabetes, Carnegie Institution of Washington, 1912, Pub. No. 176; Ueber den Stoff- und Energieumsatz bei Diabetes, Deutsch. Arch. f. klin. Med., 1913, cxi, 333.

5. Joslin, E. P.: Carbohydrate Utilization in Diabetes, The Archives Int. Med., 1915, xvi, 693.

6. Falta, W.: Zur Theorie und Behandlung des Diabetes mellitus, Med. Klin., 1914, x, 9.

7. Rolly, F.: Zur Theorie und Therapie des Diabetes mellitus, Deutsch. Arch. f. klin. Med., 1912, cv, 494.

8. Roth, N.: Ueber Mehltage bei Diabetes, Wien. klin. Wchnschr., 1912, xxv, p. 1864.

9. Allen, Frederick M.: Studies Concerning Diabetes, Jour. Am. Med. Assn., 1914, lxiii, 939; Boston Med. and Surg. Jour., 1915, clxxii, 242; New York State Jour. Med., 1915, xv, 330; Am. Jour. Med. Sc., 1915, cl, 480; Exercise, Boston Med. and Surg. Jour., 1915, clxxiii, 743; Investigative and Scientific Phases of the Diabetic Question, with Their Probable Relations to Practical Problems of Clinical Medicine, Jour. Am. Med. Assn., 1916, lxvi, No. 20, p. 1525.

consisting of a prolonged initial fast with subsequent strict regulation of all elements of the diet, has proved successful in clearing up both the urinary and the clinical symptoms in a considerable number of cases, even of very severe diabetes. The underlying principles will be discussed more fully elsewhere, but one feature considered theoretically important for the beneficial results has consisted in a diminution in the metabolism, not merely of the sugar-forming materials (carbohydrate and protein) but also of fat. The question of diminution of metabolism could be settled only by experiments in the respiration calorimeter.

2. The first dextrose-nitrogen ratio was established by Minkowski, who discovered that totally depancreatized dogs, fasting or on carbohydrate-free diet, excreted in the urine approximately 2.8 gm. of glucose for each gram of nitrogen. A constant ratio at this level indicates that 45 per cent. of the protein catabolized is being formed into glucose and excreted, and that no sugar is being formed from fat. The original interpretation was furthermore that 45 per cent. represents the maximum proportion of protein convertible into sugar. Lusk[10] and collaborators demonstrated that phlorhizinized dogs eliminate approximately 3.65 gm. of glucose for each gram of nitrogen, thus proving that at least some species of animals are capable of converting nearly 60 per cent. of the protein molecule into glucose. Also, there is no formation of sugar from fat under these conditions. Mandel and Lusk[11] demonstrated the 3.65 ratio in a human patient with severe diabetes. They urged the prognostic value of determinations of the relations of sugar and nitrogen on carbohydrate-free diet; and because the total loss of power to use carbohydrate indicated by the 3.65 ratio supposedly precluded improvement, they referred to this as the "fatal ratio." Foster and Greenwald[12] also described cases showing this ratio. For other literature, reference may be made to Lusk.[13] Inasmuch as the case described by Allard showed a fall in the ratio on fast-days, Lusk considered it no longer certain that the 3.65 ratio is necessarily permanent or fatal.

10. Lusk, G.: Phlorhizinglukosurie, Ergebnisse der Physiologie, 1912, xii, 315.

11. Mandel, A. R., and Lusk, G.: Stoffwechselbeobachtungen an einem Falle von Diabetes mellitus, mit besonderer Berücksichtigung der Prognose, Deutsch. Arch. f. klin. Med., 1904, lxxxi, 472; Diabetes Mellitus. Report on a Case, Including a New Method of Prognosis, Jour. Am. Med. Assn., July 23, 1904, p. 241.

12. Foster, N. B.: Wie hoch ist der Dextrose: Stickstoff-Quotient bei schwerstem Diabetes? Deutsch. Arch. f. klin. Med., 1913, cx, 501; Greenwald, I.: Jour. Biol Chem., 1913-14, xvi, 375; and 1914, xviii, 115.

13. Lusk, G.: Metabolism in Diabetes, The Archives Int. Med., 1909, iii, v; Note on "A Case of Pancreatic Diabetes Mellitus," by Herman O. Mosenthal, The Archives Int. Med., 1912, x, 122. Allard: Arch. f. exper. Path. u. Phar., 1907, lvii, 1.

3. The level of the respiratory quotient theoretically to be expected in diabetes has been discussed by Magnus-Levy[14] and by Lusk.[15, 16] On the basis of the newer information concerning the amino-acid content of proteins, the latter calculates that when the dextrose-nitrogen ratio is 3.65, the quotient of protein is 0.632. The formation and excretion of acetone bodies also tends to lower the quotient in a manner which can be calculated; but at the same time such acid substances may react with sodium bicarbonate to set free carbon dioxid, so that the precise theoretical value of the quotient in diabetes cannot be determined. The actual observations in phlorhizinized dogs and human patients with the 3.65 ratio are found to meet the theoretical expectations with quotients approximating 0.69. Two features of the recent literature concerning the respiratory quotient require mention in the present connection. One is the absence, in exact modern work, of the very low quotients previously found in diabetes and other conditions. Leimdörfer[17] is the only recent author who reports such low quotients; and as they are so numerous in his experiments, while his cases of diabetes were obviously of no extraordinary severity, it is apparent that something in his methods tended to give low values. Grafe and Wolf,[37] though reporting dextrose-nitrogen ratios indicating formation of sugar from fat, found no support for this hypothesis in the respiratory quotient, which was about 0.74. Technical errors, especially in connection with the oxygen measurements (Benedict[18]), may be assumed to explain the low values in the early literature. The average quotient of Benedict and Joslin's severe cases of diabetes was 0.73; and Joslin[5] presents a table of the other cases in the literature, showing the general average to be 0.73. Respiration experiments therefore stand opposed to the doctrine of sugar-formation from fat in human

14. Magnus-Levy, A.: Respirationsversuche an diabetischen Menschen, Ztschr. f. klin. Med., 1905, lvi, 83.

15. Lusk, G.: Clinical Calorimetry, Paper Eight. On the Diabetic Respiratory Quotient, The Archives Int. Med., 1915, xv, 939.

16. Williams, H. B., Riche, J. A., and Lusk, G.: Animal Calorimetry II. The Metabolism of the Dog Following the Ingestion of Meat in Large Quantities, Jour. Biol. Chem., 1912, xii, 349, 356.

17. Leimdörfer, A.: Ueber den respiratorischen Stoffwechsel des Diabetikers bei verschiedener Kostform, Biochem. Ztschr., 1912, xl, 326.

18. Benedict, F. G.: A Comparison of the Direct and Indirect Determination of Oxygen Consumed by Man, Am. Jour. Physiol., 1910, xxvi, 15; Factors Affecting Basal Metabolism, Jour. Biol. Chem., 1915, xx, 263; Metabolism During Inanition, Harvey Lectures, 1906-07.

Benedict, F. G., and Emmes, L. E.: The Basal Gaseous Metabolism in Men and Women, Jour. Biol. Chem., 1914, xviii, 139; A Comparison of the Basal Metabolism of Normal Men and Women., Proc. Nat. Acad. Sc., 1915, i, 104; A Comparison of the Basal Metabolism of Normal Men and Women, Jour. Biol. Chem., 1915, xx, 253; Benedict, F. G., and Smith, H. M.: The Metabolism of Athletes as Compared with Normal Individuals of Similar Height and Weight, Jour. Biol. Chem., 1915, xx, 243.

diabetes. The second feature to be mentioned consists in the unexpectedly high quotients shown by some cases of severe diabetes, as observed independently by Benedict and Joslin and by observers in the Russell Sage laboratory. Table 5 in the paper by Joslin[19] contains the record of a patient with severe diabetes, fasting except for from 2 to 5 gm. protein and from 15 to 24 gm. alcohol daily, yet with respiratory quotient of from 0.74 to 0.76. Joslin[19] mentions other observations of a rise in the respiratory quotient of severely diabetic patients during fasting, even up to the neighborhood of 0.8. The cause of such high quotients is not known. Nothing analogous has been described in the study by Benedict[20] and earlier workers of cases of prolonged fasting; they found that in normal persons the quotient falls and remains low during fasting. Aside from the presumably scanty supply of stored carbohydrate, Joslin has suggested the acetone bodies as the only known material capable of raising the quotients of diabetic patients by combustion under these conditions.

4. The total metabolism in diabetes has been an actively discussed subject. The earlier literature is critically reviewed by Benedict and Joslin.[4] It has been universally agreed that the basal metabolism of mild cases of diabetes is normal, and that of most severe cases is found increased when reckoned per kilogram of body weight. But in addition to accuracy in measuring the gas exchange and heat production, there is the further requirement of an accurate basis of comparison between diabetics and other persons. Magnus-Levy[14] called attention to the fact that the emaciation of most patients with severe diabetes alters the relation of their body weight and surface, and suggested that it might be more nearly correct to compare on the basis of the original normal weight of the diabetics. Benedict and Joslin rejected this proposal, because the surface of the diabetic apparently diminishes with the body mass and the skin shows no tendency to fall in folds or wrinkles. They chose, as the most accurate means available, to compare groups of patients with severe diabetes with groups of normal and mildly diabetic persons, as nearly like them as possible in size and figure. On this basis they estimated that their severely diabetic patients showed an increase of from 6 to 7 per cent. in carbon dioxid excretion, of from 16 to 21 per cent. in oxygen consumption, and of about 15 per cent. in heat production. Lusk[21] criticized the findings in various particulars, and by recalculation concluded that the metabolism

19. Joslin, E. P.: Present-Day Treatment and Prognosis in Diabetes, Am. Jour. Med. Sc., 1915, cl, 485.

20. Benedict, F. G.: The Influence of Inanition on Metabolism, Carnegie Institution of Washington, 1907. A Study of Prolonged Fasting, Carnegie Institution of Washington, Pub. No. 203, 1915.

21. Lusk, G.: Science, 1911, N. S., xxxiii, 433-434.

represented was not 15 per cent. but only 5 per cent. above normal. Benedict and Joslin[4] in their second publication added to the number of diabetics and especially of control subjects studied, and reckoned that the basal metabolism in this group of diabetics was approximately 20 per cent. above normal. Lusk[22] calculated that an increase of from 5 to 10 per cent., and in exceptional instances 15 per cent., above normal was shown. Leimdörfer[17] found an increase of metabolism in severe cases of diabetes on the basis both of the weight and of the body surface as figured by Meeh's[23] formula. Diminution of metabolism observed after oat or vegetable days was held to confirm this interpretation. Rolly[7] found in severe diabetes an increased oxygen consumption per kilogram of body weight, especially soon after admission to hospital; after a period of treatment the findings were lower. Seib[24] also reported the respiratory metabolism increased in proportion to the severity of the case. In Paper 10 of the present series is described the height-weight formula for calculating the body surface, which has been found more accurate and reliable for this purpose than the Meeh formula, especially when the body form varies in any way from the average normal. It is possible by this formula to recalculate any results recorded in the literature, wherever the height and weight of the subject have been given. It is believed that the second of the requirements mentioned is thus fulfilled, and that, granting accurate experimental observations, a correct basis of comparison is afforded between diabetic and other subjects in a manner not possible heretofore.

The causes of the departure of the diabetic basal metabolism from the normal are partly known, perhaps partly unknown. It may be taken as an axiom that the diabetic, excreting sugar formed from protein, must catabolize more protein during fasting than the nondiabetic person under identical conditions, and that the specific dynamic action of protein will therefore give rise to a higher metabolism in the diabetic, unless some other factor prevents or neutralizes the effect of the protein. The suggestion was offered by Benedict and Joslin that acidosis may be a cause of increased metabolism. They observed the discrepant fact that a sudden slight acidosis is accompanied by an increase of metabolism out of proportion to that noted with prolonged high acidosis. At the present time the subject of acidosis is a confused one;

22. Lusk, G.: Animal Calorimetry XI. An Investigation into the Cause of the Specific Dynamic Action of the Foodstuffs, Jour. Biol. Chem., 1915, xx, 555.

23. Meeh, K.: Oberflächenmessungen des menschenlichen Körpers, Ztschr. f. Biol., 1879, xv, 425.

24. Seib, K.: Experimentelle Untersuchungen über den respiratorischen Gaswechsel bei Diabetes mellitus nach Eiweisszufuhr und bei Hyperthermie, Zentralbl. f. Physiol., 1913-14, xxvii, 930.

it can no longer be regarded as a simple condition resulting from lack of carbohydrate.[9] Greater clearness concerning the effect upon metabolism may now result from separate consideration of individual factors present. First, some or all cases of sudden acidosis are accompanied by increased protein breakdown, which may be a cause of increased metabolism. Second, if acidosis in the strict sense increases metabolism, not only should subjects with high acidosis show higher metabolism than those with low acidosis, but also alkali given in sufficient quantity should in suitable cases cause a fall in metabolism. Third, it is possible that acetone bodies, even in the form of neutral salts, may stimulate metabolism if present in excess in the blood and tissues. Here the suggestion is analogous to that of Lusk[25] that diabetic lipemia may be a cause of increased metabolism. Increased concentration of combustible materials may be expected to result in a stimulation of metabolism, unless the power of combustion is diminished, or the specific dynamic action otherwise prevented. At the same time, the narcotic and depressant action of the acetone bodies might conceivably tend to depress metabolism, especially in the long-standing cases with high ketonemia. Other influences unquestionably tend to depress metabolism in such cases, as for example undernutrition and muscular relaxation. The effect of muscular mass and tone is evident in the higher metabolism of men as compared with women, and of athletes as compared with other men (Benedict[18] and collaborators); and Lusk[22] has shown that mere prolonged cage life may reduce a dog's basal metabolism by 16 per cent., though the diet and weight remain the same. The subject will be further considered below.

An account of the metabolism in a case of diabetes of remarkable intensity was recently published by Geyelin and DuBois.[26] To facilitate reference, some of the findings in this case are briefly reproduced in Table 1.

METHODS AND CALCULATIONS

The procedures used for the chemical determinations were as follows: for the blood-sugar, the method of Lewis and Benedict;[27] for the urinary sugar, titration with Benedict's solution; for nitrogen, the usual Kjeldahl method; for ammonia, the Folin method; for acetone bodies, the Shaffer method. Foods were weighed raw and the composition estimated from the Atwater-Benedict tables, unless special mention is made of analyses. For separating the twenty-four-hour urines,

25. Lusk, G.: The Influence of Food on Metabolism, Proc. Am. Soc. Biol. Chem., December, 1914; Jour. Biol. Chem., 1915, xx, 8.

26. Geyelin, H. R., and Du Bois, E. F.: Jour. Am. Med. Assn., 1916, lxvi, No. 20, 1532.

27. Lewis, R. C., and Benedict, S. R.: A Method for the Estimation of Sugar in Small Quantities of Blood, Jour. Biol. Chem., 1915, xx, 61.

TABLE 1.—The Case of Cyril K. (Summary from Geyelin and DuBois)

Date	Food				Urine				Respiratory Quotient	Calories per Sq. M. per Hour Linear Formula	Blood	
	Total Calories	Fat. Gm.	Nitrogen, Gm.	Carbohydrate, Gm.	Nitrogen, Gm.	Glucose, Gm.	Dextrose-Nitrogen Ratio	Beta-oxybutyric, Gm.			Glucose, Mg. per 100 c.c.	CO_2 Combining Capacity, mm.
Dec. 8-9	138*	0	0	0	27.9	74.9	2.68	43.8	....	....	313	30.4
Dec. 9-10	336*	0	0	0	29.8	78.3	2.61	31.6	.....	....	...	....
Dec. 10-11	0	0	0	0	24.8	71.2	2.86	....	.....	....	310	26.6
Dec. 11-12	405	17.7	2.8	41.5	30.6	108.0	2.47	60.0	.....	....	312	21.1
Dec. 12-13	1,058	69.6	8.0	50.0	31.5	112.0	1.80	53.0	.....	....	...	22.7
Dec. 13-14	568	38.5	8.8	30.0	35.1	118.7	1.7	0.9		....	.	22.5
Dec. 14-15	936	51.2	9.8	53.3	37.7	118.5	1.75	65.2	....	....	...	....
Dec. 15-16	934	41.0	19.0	23.5	36.4	167.9	3.97	70.9	0.687	45.74	...	20.0
Dec. 16-17	158	5.6	15.9	0.1	38.3	153.4	4.01	75.1	0.714	42.64	...	19.6
Dec. 17-18	194	2.9	6.3	0.4	36.3	140.3	3.87	87.4	.....	....	...	....
Dec. 18-19	0	0	0	0	20.0	55.1	2.76	58.5	0.707	40.8	150	35.1 55.1
Dec. 19-20	0	0	0	0	16.7	44.3	2.65	56.8	.....	....	...	49.7
Dec. 20-21	36	0	1.6	1.0	14.1	35.3	2.44	41.2	0.721	37.0	177	52.5
Dec. 21-22	60	0	3.2	1.6	14.4	39.7	2.65	26.2	.....	....	170	....
Dec. 22-23	80	0.1	3.4	5.6	18.3	26.0	1.12	11.0	0.731	35.9	181	52.9
Feb. 16	.....	....	....	....	....	0	0	0	0.915	25.4	...	....

* Alcohol. † After breakfast, not basal.

patients emptied the bladder at precisely 5 a. m. daily, and care was taken that no urine was lost under any conditions. The entire planning and organization of the ward was for the purpose of exact metabolic studies, and accuracy in matters of dietary control, collection of excreta and other details is fully assured.

At the time of the diabetes experiments the calorimeter was in perfect working order and the staff was well trained. Alcohol checks lasting two or three hours gave respiratory quotients in which even the third decimal place was not far from the theoretical. In experiments on man it has never before been felt advisable in this laboratory to print more than two significant figures in the respiratory quotients, but it has seemed justifiable to use three in the present work, both on account of the extreme care in the experiments and of the importance of the third decimal point in some of the calculations. In no case are deductions made from single hours but only from the averages of periods as long as possible.

The calculations concerning the metabolism where there was sugar formation from protein followed the method described by Lusk.[16] In the normal metabolism each gram of nitrogen in the urine indicates the combustion of 6.25 gm. protein with the liberation from this protein of 26.51 calories, 9.35 gm. carbon dioxid and the absorption of 8.45 gm. oxygen. It is obvious that if part of this protein molecule is unoxidized in the diabetic organism and is excreted in the urine, all of these figures will be lowered by exactly the number of calories and grams of carbon dioxid and oxygen lost in the glucose. With a dextrose-nitrogen ratio of 3.65 to 1, 1 gram of nitrogen in the urine indicates the combustion of 6.25 gm. protein with the liberation of 26.51 minus 13.47 calories, 9.35 minus 5.35 gm. carbon dioxid, and the absorption of 8.45 minus 3.89 gm. oxygen. When the dextrose-nitrogen ratio is lower, the calculation is easily made as follows: The calories, carbon dioxid and oxygen ascribed to the metabolism of protein are calculated from the number of grams of nitrogen excreted per hour by using the normal factors given by Lusk.[16] Knowing the number of grams of glucose excreted per hour, one can make the proper subtractions, since each gram of glucose represents a loss of 3.692 calories, 1.467 gm. carbon dioxid and 1.067 gm. oxygen. In this way it is possible to determine the nonprotein respiratory quotient and the heat production by the method of indirect calorimetry. If there is no glycosuria, or if the sugar of the urine is all derived from ingested carbohydrate, the calculations are exactly the same as for normal persons. No attempt has been made to calculate the combustion of the acetone bodies or the ingested alcohol, the conditions of experimentation rendering this impossible.

For reasons fully stated in previous papers, the method of indirect calorimetry is used as the standard, and the divergence of the direct calorimetry from this is expressed in terms of percentage. In typhoid fever, exophthalmic goiter, anemia and cardiorenal disease there is a tendency for the direct calorimetry to average from 2 to 3 per cent. lower, probably on account of heat lost through the warming of the bed and clothing, possibly also because of errors in measuring the average temperature of the body. This same tendency to a small minus error is seen in most of the diabetes experiments. The total divergence of the two methods in the present work is 2.3 per cent., and the average

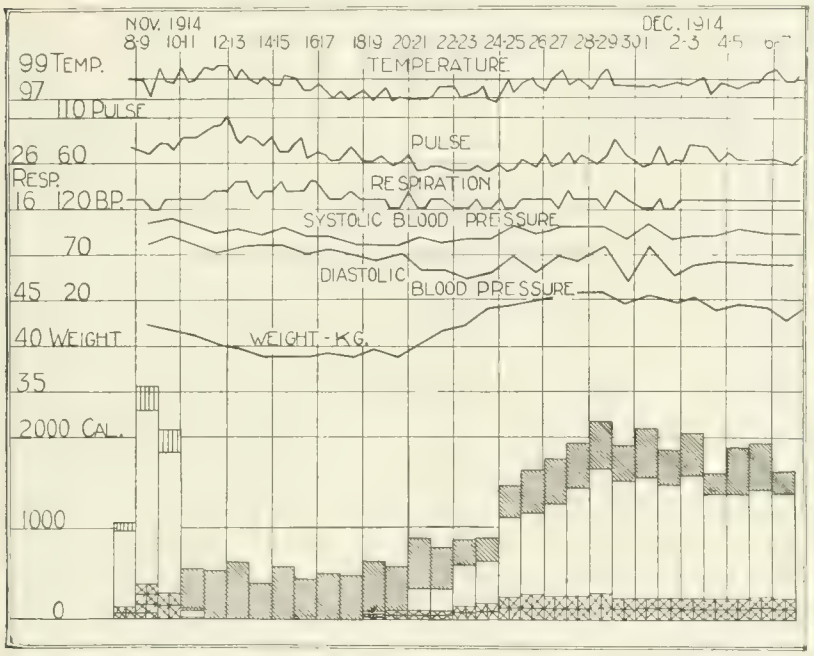

Fig. 1 (Gerald S.).—Clinical findings shown graphically. The columns at the base represent the calories of the food; vertical lines, carbohydrate; crossed lines, protein; diagonal lines, alcohol; blank space, fat calories.

divergence in individual experiments is plus or minus 5.5 per cent. The agreement of the two methods is therefore satisfactory, and would be still closer but for the peculiar divergence of the findings in the case of Gerald S. on the last day of the prolonged fast and during the following two weeks. This point is discussed in the history of his case, which follows.

CASE REPORTS

Case 1.—Gerald S. (severe diabetes), plumber, aged 17, unmarried. Healthy family and past life, habits good, normal weight 60 kg. Polyuria and polydipsia were noticed January, 1914. Entered Bellevue Hospital June, 1914, weighing

TABLE 2.—Gerald S.:—

Date, 1914	Food						Urine N, Gm.	Urine Glucose, Gm.
	Total Calories	Protein, Gm.	Fat, Gm.	Carbo., Gm.	Alcohol, Gm.	Food N, Gm.		
Nov. 8- 9	1,056*	31.2	91.7	18.3	....	4.99	.....	.....
Nov. 9-10	2,550	96.2	204.4	62.2	....	15.40	.....	.....
Nov. 10-11	2,078	67.0	166.4	62.1	....	10.72	14.71	106.43
Nov. 11-12	540	1.3	9.5	2.3	62.6	0.20	10.76	41.95
Nov. 12-13	526	0	0	0	75.2	0	10.40	24.49
Nov. 13-14	614	0	0	0	87.7	0	10.87	15.68
Nov. 14-15	380	0	0	0	54.3	0	9.30	8.91
Nov. 15-16	555	0	0	0	79.3	0	11.10	6.53
Nov. 16-17	438	0	0	0	62.6	0	8.52	7.10
Nov. 17-18	497	0	0	0	71.0	0	8.24	2.80
Nov. 18-19	468	0	0	0	66.8	0	6.11	0.76
Nov. 19-20	622	12.2	1.8	2	79.3	1.95	7.12	0
Nov. 20-21	578	14.5	2.4	2	71.0	2.32	5.72	0
Nov. 21-22	892	24.1	25.8	2	79.3	3.85	8.41	0
Nov. 22-23	787	21.0	25.1	2	66.8	3.36	6.45	0
Nov. 23-24	878	34.6	47.7	2	41.8	5.53	9.13	0
Nov. 24-25	887	37.6	50.5	2	37.6	6.01	7.23	0
Nov. 25-26	1,464	57.9	95.9	3	50.1	9.26	6.56	0
Nov. 26-27	1,635	65.7	95.6	2	71.0	10.51	8.20	0
Nov. 27-28	1,752	61.1	110.8	2	71.0	9.77	7.17	0
Nov. 28-29	1,929	61.1	130.0	2	71.0	9.77	7.18	Trace
Nos. 29-30	2.175	68.4	151.5	2	75.0	10.75	8.58	Trace
Nov. 30-Dec. 1	1,795	56.0	140.6	2	41.8	8.96	6.89	Trace
Dec. 1- 2	2,077	55.1	146.7	2	75.2	8.81	6.73	1.71
Dec. 2- 3	1,845	57.3	138.9	2	50.1	9.16	5.72	0
Dec. 3- 4	2,034	55.7	148.1	2	66.8	8.91	5.94	Trace
Dec. 4- 5	1.606	53.9	126.6	2	33.4	8.62	5.49	0
Dec. 5- 6	1,893	53.4	126.2	2	75.2	8.54	7.23	0
Dec. 6- 7	1,942	56.9	130.0	2	75.2	9.10	6.30	0
Dec. 7- 8	1,614	54.4	127.2	2	33.4	8.70	6.61	0
Dec. 8- 9	1,872	56.4	128.9	2	66.8	9.02	6.95	0
Dec. 9-10	2,022	56.2	146.6	2	66.8	8.99	6.56	0
Dec. 10-11	2,111	54.8	145.9	2	66.8	8.76	7.28	0
Dec. 11-12	2,191	52.9	166.0	2	66.8	8.46	7.06	0
Dec. 12-13	2,308	60.0	175.6	2	66.8	9.60	7.73	0
Dec. 13-14	2,208	61.1	164.3	2	66.8	9.77	7.17	0
Dec. 14-15	2,221	59.2	166.6	2	66.8	9.74	6.22	0
Dec. 15-16	2,368	68.4	172.1	2	75.2	10.94	7.45	0
Dec. 16-17	2,532*	46.4	211.9	2	58.5	7.49	.....	.....

* Not complete.

—Clinical Data

Urine NH_3, Gm.	Beta-oxybutyric, Gm.	Total Acetone Bodies as Beta-oxybutyric Gm.	Feces N† Gm.	Excreta N, Gm.	Nitrogen Balance, Gm.	Water Intake, Gm.	Urine Volume, c.c.	Body Weight, c.c.	Blood Sugar, Per Cent
....	.....	.....	.....	.....	.....	1,450	1,300	.....	.....
?	.....	.....	.....	.....	.....	2,220	?	42.19	....
3.40	7.128	13.218	.....	15.78	— 1.07	2,960	3,526	.....	.....
4.75	2.071	3.811	?	10.76	—10.75	3,705	3,460	41.27	[illegible]
4.46	1.815	2.517	0	10.40	.....	2,398	1,909	40.15	....
3.08	0.584	0.990	0	.....	.. ....	2,065	2,700	3.026	.....
2.18	0.616	1.048	0	.....	... ...	2,197	1,836	38.97	... ..
1.50	0.475	1.155	0	.....	.....	2,450	2,563	38.92	[illegible]
0.80	0.416	0.656	0	.....	.....	1,570	1,428	38.80	.....
0.71	0.308	0.588	0	.....	. .....	2,385	2,128	39.05	0.284
0.40	0.064	0.164	0	.....	... ...	1,725	1,153	38.74	....
0.57	0.436	0.592	0.234	7.35	.....	2,685	3,115	39.55	[illegible]
0.42	0.186	0.322	0.29	6.01	.....	2,185	1.980	38.74	.....
0.51	0.208	0.373	0.46	8.87	... ...	2,883	2,360	40.22	.....
0.48	0.341	0.613	0.40	6.85	.....	2,375	1,940	41.87	0.156
0.49	Lost	.....	0.66	9.79	.....	2,235	1.643	42.66	.....
0.50	0.258	0.423	0.72	7.95	.....	1,500	1,835	44.02	0.182
0.44	0.250	0.358	1.11	7.49	+ 1.77	1,550	1,200	44.14	.....
0.68	.....	.....	1.11	9.31	+ 1.20	2,500	3.540	.....	.....
0.46	.....	.....	1.11	8.28	+ 1.49	2,450	3,220	45.15	.....
0.50	.....	.....	1.11	8.29	+ 1.48	2,175	2,955	45.64	0.167
0.58	.....	.....	1.11	9.69	+ 1.06	2,780	4,005	45.27	.....
0.46	.....	.....	1.11	8.00	+ 0.96	1,870	2,225	44.27	.....
0.82	.....	.....	1.11	7.84	+ 0.97	1,795	3,085	45.35	0.208
0.88	.....	.....	0.945	6.67	+ 2.49	2,100	2,473	44.76	.....
0.55	.....	.....	0.945	6.885	+ 2.025	2,500	3,815	45.42	.....
0.30	.....	.....	0.945	6.435	+ 2.185	2,050	3,178	43.94	.....
0.57	.....	.....	0.95	8.18	+ 0.36	2,980	4,525	44.77	.....
0.44	.....	.....	0.95	7.28	+ 1.82	2,875	3,980	43.82	0.177
0.38	.....	.....	0.95	7.56	+ 1.14	1,455	2,327	42.58	.....
0.52	.....	.....	0.95	7.90	+ 1.12	2,010	3,610	43.32	.....
0.35	.....	.....	1.34	7.90	+ 1.09	3,070	3,750	42.61	.....
0.55	.....	.....	1.34	8.62	+ 0.14	3,000	3,880	41.74	.....
0.49	.....	.....	1.34	8.40	+ 0.06	3,250	3,865	42.43	.....
0.68	.....	.....	1.34	9.07	+ 0.53	2,510	3,110	42.30	... .
0.75	.....	.....	1.34	8.51	+ 1.26	2,730	3.010	42.36	0.113
0.60	.....	.....	1.34	7.56	+ 2.18	2,850	3,650	42.55	... .
0.71	.....	.....	1.34	8.79	+ 2.15	2,800	3,030	41.79(?)	...
....	.....	.....	....	....	.....	2,605	1,565	42.67	.....

† Feces N calculated as 12% of Food N, up to November 26.

47 kg. After twenty-five days he was discharged weighing 57 kg. Glycosuria was said to have been 10 per cent. on admission, 5 per cent. on discharge. A dose of salts taken October 24 left him very weak, and thereafter he lost weight and strength rapidly. He was admitted to Rockefeller Hospital Nov. 7, 1914. Height 172 cm., weight 41.6 kg., extremely weak. Heart, lungs and abdomen negative; blood-pressure 85 systolic, 75 diastolic; clinical picture of acidosis, with drowsiness and increased respiration threatening coma. His diet containing

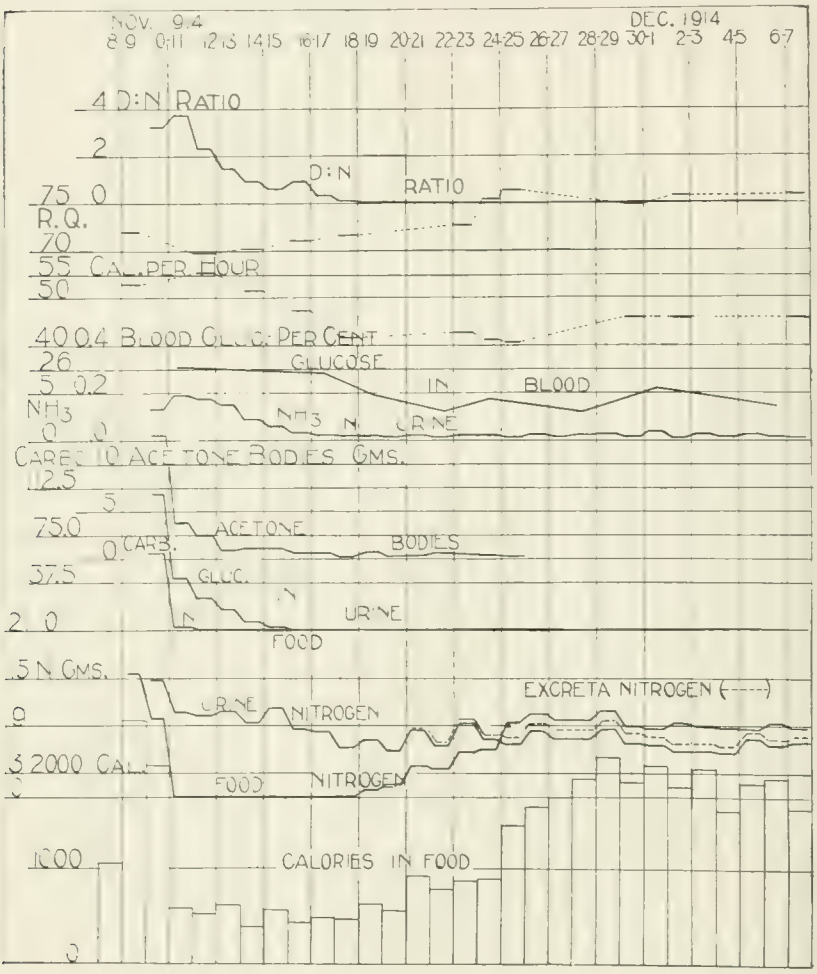

Fig. 2 (Gerald S.).—Laboratory findings shown graphically.

carbohydrate was continued, and he was transferred next day to the Russell Sage metabolism ward at Bellevue Hospital, where he remained until the close of the metabolism experiments, then returned to the Rockefeller Hospital.

The diet shown in Table 2 was all he could eat on November 8 to 10 inclusive. At 6 a. m. on November 11 he received 50 c.c. cream, then developed nausea without vomiting. Fasting was begun at this time because of the complete repugnance to food and the dangerously threatening coma symptoms. No bicarbonate was given except 10 gm. on November 11. The fast lasted eight days,

and the condition cleared up, as shown in the table. Alcohol was given in the form of whisky during the fast, in quantities just short of producing any discomfort or intoxication symptoms. Notwithstanding the extreme initial weakness, the clinical condition perceptibly improved during the fast. The first food added to the alcohol after the fast was protein—eggs at first, later meat. More protein and fat were gradually added, until the unduly high diet of over fifty calories per kilogram of weight was reached. Bulk was contributed to the diet by the use of from 750 to 1,000 gm. of thrice-boiled vegetables daily, some samples of which were analyzed for carbohydrate. The rapid gain in weight shortly after the fast was due to the water retention common in such patients. Improvement continued in subsequent treatment. The carbohydrate tolerance remained low, but the patient became able to exercise freely, and he and his parents considered him fit for work. For this reason he refused to be further controlled, and was dismissed from the hospital and from all further supervision, with due warning of the consequences. The discharge was on Feb. 8, 1915, the diet at that time being about 1,400 calories, with no glycosuria or ketonuria, and the body weight 44 kg. He progressed rapidly downward and died March 9, 1915.

Case 2.—William G. (severe diabetes), printer, age 29, married. Family, personal history and habits negative. Figure thin; normal weight from 66 to 69 kg. Thirst and dry mouth noticed in June, 1913. Progress was steadily downward in spite of treatment. Entered Presbyterian Hospital July 25, 1914. His condition there was dangerous on carbohydrate-free diet and worse when it was attempted to add carbohydrate. The dextrose-nitrogen ratio was found to be about 3. He was transferred to Rockefeller Hospital on July 28. Height 179 cm., weight 50 kg. Physical examination negative. Table 3 contains part of the laboratory data for this period. Carbodydrate of food was determined only by calculation. Other food values for the first two days are calculated. After that, nitrogen and fat were analyzed in food and feces.

Thus the emaciated patient, spending most of the twenty-four hours in bed and the rest of each day sitting limply in a chair, was unable to maintain his body weight even on utilizable calories in excess of the needs of a normal person of equal weight. The excess of fat failed to prevent nitrogen loss. Yet high protein feeding is known to aggravate diabetes, even though temporary nitrogen equilibrium is attained. This is the old dilemma. As soon as the appetite partly failed, on August 1, the nitrogen deficit became large. Fasting had to be inaugurated on August 2 because of symptoms of beginning coma. Along with the fall in glycosuria, within two days the level of nitrogen excretion characteristic of advanced inanition was attained. Feeding with green vegetables was commenced August 7. Gradual increase of vegetables up to August 12 showed a carbohydrate tolerance of 38.5 gm. Other food was then given, and there seemed to be satisfactory improvement, with glycosuria and ketonuria absent as usual. The case then differed from others in that a gradual loss of tolerance manifested itself; diagnosis was impossible for several months, but the apparent explanation of the trouble was at length found in pulmonary tuberculosis. Vain attempts were made several times to increase strength by high feeding with disregard of glycosuria. In January, 1915, with no sign of tuberculosis, the patient spent some time in the Russell Sage metabolism ward for investigation before and after such a period of high diet

TABLE 3.—William G.: Clinical Data During First Part of Stay in the Rockefeller Hospital

Date	Body Weight, Kg.	Water Intake, c.c.	Urine						Nitrogen Balance*	Food					Sodium Bicarbonate, Gm.	Calcium Carbonate, Gm.
			Volume, c.c.	Acetone Bodies as Beta-oxybutyric Acid, Gm.	Ammonia Nitrogen, Gm.	Dextrose Gm.	Dextrose-Nitrogen Ratio	Total Nitrogen, Gm.		Nitrogen, Gm.	Carbohydrate, Gm.	Alcohol, Gm.	Calories			
													in Food	Available†		
July 29-30.....	49.4	1,800	3,424	26.05	2.88	61.63	2.6	23.27	— 6.86	17.29	6.9	...	2860.7	2448.1	..	20
July 30-31.....	47.4	2,540	2,570	20.51	2.16	64.99	3.3	17.48	— 0.66	17.70	11.5	...	2693.9	2297.6	20	20
July 31-Aug. 1	47.0	2,200	2,970	19.69	2.73	58.24	2.7	20.49	+ 0.39	21.78	7.7	30	3135.5	2762.6	20	20
August 1-2.....	47.4	2,810	3,165	38.62	3.48	60.46	2.4	24.36	- 12.63	12.61	5.8	30	2730.9	2261.2	20	20
August 2-3.....	47.4	2.642	1,285	15.56	4.25	17.85	1.2	14.83	- 15.71	.....	....	102	714.0	593.9	30	20
August 3-4....	48.0	1,950	2,185	8.80	2.08	1.93	0.26	7.22	.....	.....	....	97	682.5	592.9	40	20
August 4-5.....	48.4	1,870	1,840	2.47	0.44	2.04	0.34	5.99	.....	.....	....	80	560.0	499.3	10	5
August 5-6.....	48.2	2,092	2,815	2.09	0.88	0	....	7.04	.....	.....	....	102	714.0	656.0	..	..
August 6-7.....	47.6	2,722	2,100	2.97	1.07	0	....	10.20	.....	.....	....	92	644.0	582.2	..	..
August 7-8.....	47.0	2,785	2,365	4.95	1.16	0	....	6.72	— 7.26	0.34	5.8	82	610.3	535.0	..	..
August 8-9.....	47.2	2,545	1,625	3.10	1.06	0	....	7.66	— 7.69	0.85	15.7	85	688.6	626.2	..	..

* Average daily N in feces 0.876 gm.
† Calories lost in urine and feces subtracted from calories of diet.

(Table 4). He was subjectively and objectively so much better when kept free from glycosuria and ketonuria, that this was done nearly constantly until March 11, 1915. Then the course of the tuberculosis was becoming very rapid. Death occurred from diabetes and bronchopneumonic tuberculosis on March 22, 1915.

CASE 3.—Joseph U. (severe diabetes), manufacturer, aged 44, married. His family, personal history and habits were negative. Normal weight 75 kg. In 1907, loss of weight, and medical diagnosis of diabetes. At first kept free from glycosuria occasionally by treatment, but it has been continuous for the past three or four years. Emaciation and weakness have been the principal symptoms. Patient was bedridden for the six weeks preceding admission to hospital. He was brought on a cot from his home in Indiana and entered Rockefeller Hospital Nov. 28, 1914. Height 179 cm., weight 44.2 kg. Physical examination was negative, except for emaciation and a yellow tinge like pernicious anemia, which diagnosis was excluded by blood examination. Blood pressure not certain. On January 18, when he appeared much stronger and was beginning to sit up a little, systolic blood pressure was 76, diastolic 60. Glycosuria and ketonuria heavy. Ammonia nitrogen 2.5 gm on November 28-29, 2.78 gm. on November 29-30. No symptoms of acidosis.

Treatment was conducted by Dr. Stillman. The patient fasted November 30 to December 7, inclusive, receiving 70 c.c. whisky daily, and on December 7 receiving also 500 gm. thrice-boiled vegetables. Eggs and butter were added gradually until on December 10 the diet contained 52 gm. protein, 95 gm. fat, 100 c.c. whisky, and 500 gm. thrice-boiled vegetables. On this day a glycosuria of 9.5 gm. appeared. The strength and well-being had improved from the outset; but though ketonuria had diminished, it had never cleared up satisfactorily. The carbohydrate tolerance was literally nothing. Details will be published elsewhere. Briefly, it was necessary to keep him on a diet of about 700 calories daily, about half of which was alcohol, until February 3. He was warm and quiet in bed except for short daily periods. The weight on February 3 was 40.3 kg., and strength continued to improve. It was toward the close of this prolonged undernutrition that the calorimeter tests were made, on January 31 and February 1. It then became possible to increase the diet somewhat, but fast-days were still used frequently. The ferric chlorid reaction slowly diminished to traces, but did not become regularly negative until the latter part of May. The patient was discharged June 28, 1915, at precisely his initial weight, namely, 44.2 kg., with urine normal on a diet of 80 gm. protein, 15 gm. carbohydrate and 1,950 calories. He has since conducted his business. Carelessness with his diet brought back glycosuria and required his return to the hospital on Oct. 17, 1915; but the condition was much more favorable than before and the tolerance higher on discharge from the hospital this time (Jan. 18, 1916) than on the previous occasion.

CASE 4.—Edward M. (moderately severe diabetes), customs inspector, aged 34, married. His family, personal history and habits were negative, except for chronic indigestion and constipation since the age of 22. Normal weight 80 kg. In July, 1913, occurred sudden attack of dizziness, colic, vomiting and diarrhea, with fever for one day. From that time on he was constantly thirsty and lost weight and strength. Diabetes diagnosed in September. Under inefficient treatment he was sugar-free for only two periods of one week each. Entered Rockefeller Hospital July 15, 1914. Weight 60.4 kg. Highly neurasthenic, but no serious emaciation or acidosis. Physical examination negative except for sallow color and enlarged liver. On restricted diet there was marked ketonuria and a negative carbohydrate balance of about 12 gm. Four days of fasting from July 18 to 21, inclusive, were required to stop glycosuria. Feeding was begun on July 23, with vegetables containing 12.2 gm. carbohydrate.

TABLE 4. WILLIAM G.: CLINICAL DATA DURING STAY AT BELLEVUE HOSPITAL JANUARY 10 TO 15

Date	Body Weight, Kg.	Water Intake, c.c.	Urine						Nitrogen Balance	Food			
			Volume, c.c.	Diacetic Acid	Ammonia Nitrogen, Gm.	Dextrose, Gm.	Dextrose-Nitrogen Ratio	Total Nitrogen, Gm.		Nitrogen, Gm.	Carbohydrate, Gm.	Alcohol, Gm.	Calories
Jan. 10-11	43.3	2,130	1,465	....	1.48	0	....	5.27†	−0.17	5.8	...	57.4	1,775
Jan. 11-12	43.2	1,910	1,177	++	1.60	0	....	6.47	+1.14	9.78	0.6	30.6	2,016
Jan. 12-13	43.3	2,650	1,995	++	2.81	11.4	1.27	8.49	+1.13	10.93	0.6	57.4	2,441
Jan. 13-14	....	2,350	2,520	++	2.76	15.3	2.02	7.18	+1.99	10.42	0.6	57.4	2,250
Jan. 14-15	44.9	3,100	3,665	++	4.05	23.0	2.28	9.63	+1.73	12.91	1.0	57.4	2,738
Jan. 15-16*	44.0	1,150	876	....	1.18	9.9	3.93	2.42	.....	4.41	0.4	11.5	902
Jan. 16-17	42.8	1,150	2,500	++	....	43.8	3.14	13.91	−3.96	11.3	...	20.0	1,811
Jan. 17-18	42.0	1,335	2,770	++	3.40	42.8	3.10	13.82	−3.19	12.08	...	20.0	2,305
Jan. 18-19	40.8	750	2,775	++	....	46.7	3.44	13.59	−2.96	12.08	...	22.5	2,183
Jan. 19-20	40.6	1,850	2,925	++	....	69.6	....	.....	.....	14.3	2.2	20.0	2,369
Jan. 20-21	....	2,700	4,385	++	....	76.7	3.82	20.1	−6.51	14.29	...	20.0	2,335
Jan. 21-22	42.4	4,030	4,700	++	....	45.	....	.....	.....	15.15	2.2	22.5	2,508
Jan. 22*	43	2,000	1,390	++	....	8.8	3.15	2.81	−2.81	.....	...	40.0	280

* Incomplete. † Only for the calorimeter periods.

TABLE 5.—FELIX K.: CLINICAL DATA

Date	Total Calories	Fat, Gm.	Carbo., Gm. in Food	Glucose, Gm. in Urine	N in Food, Gm.	N in Urine, Gm	Body Weight, Kg.	Urine Volume, c.c.	Remarks
1/14/14	2,046	155.4	57.7	12.05	14.2	12.13	.....	820	
1/15/14	2,016	145.4	62.5	21.50	15.8	18.61	.....	1,000	
1/16/14	2,092	163.0	62.4	12.50	12.5	12.61	.....	920	
1/17/14	1,989	141.6	64.3	13.80	15.6	14.79	56.51	1,180	
1/18/14	2,304	177.7	58.2	10.00	16.0	15.19	....	1,300	
1/19/14	2,085	149.0	64.3	6.45	16.9	11.99	56.33	940	
1/20/14	1,964	140.1	62.9	0	15.6	15.52	.....	1,580	
1/21/14	2,369	181.8	59.8	9.65	16.5	16.08	57.52	1,380	
1/22/14	2,667	216.4	60.4	9.11	15.8	12.16	56.52	1,170	
1/23/14	2,852	236.5	59.8	5.88	15.9	13.90	.....	1,360	
1/24/14	2,684	218.5	59.8	8.08	15.9	12.39	57.07	1,300	
1/25/14	3,138	247.4	59.8	5.68	16.0	10.31	.....	1,040	
1/26/14	2,733	173.7	59.8	7.14	16.1	11.77	56.76	1,360	
1/27/14	2,773	178.3	60.0	8.70	15.9	10.54	.....	1,200	
1/28/14	3,059	183.3	59.8	5.88	16.0	12.33	57.01	1,120	
1/29/14	921	76.7	20.8	0	4.7	9.36	.....	1,330	
1/30/14	2,986	179.9	60.5	0	16.2	13.84	56.98	1,460	
1/31/14	3,458	180.0	59.7	0	16.1	13.28	.....	1,520	
2/ 1/14	3,492	182.1	61.9	Trace	16.5	13.84	.....	1,600	
2/ 2/14	3,488	182.8	60.5	0	16.2	14.01	57.97	1,910	
2/ 3/14	3,492	203.8	60.5	6.88	16.2	12.95	.....	2,220	
2/ 4/14	3,579	192.2	60.5	8.08	16.5	11.77	58.76	1,860	
2/ 5/14	3,580	192.2	60.7	5.68	16.3	11.54	.....	1,640	
2/ 6/14	3,615	197.3	60.5	0	15.9	10.65	.....	1,400	
2/ 7/14	3,663	201.5	59.7	6.90	16.4	13.34	58.25	1,330	
2/ 8/14	3,620	186.3	60.5	10.00	16.3	11.21	.....	1,140	
2/ 9/14	3,310	181.6	62.3	8.34	16.2	13.17	.....	1,180	
2/10/14	982	81.7	20.8	0	5.3	9.92	58.17	1,300	Green day
2/11/14	929	77.1	20.8	0	5.1	9.33	57.56	1,155	Green day
2/12/14	2,138	124.1	178.1	13.80	9.9	11.59	57.84	1,515	Oatmeal day
2/13/14	2,177	127.1	178.1	19.22	10.3	10.87	57.93	1,580	Oatmeal day
2/14/14	2,171	126.7	178.1	31.08	10.2	10.54	57.80	1,930	Oatmeal day
2/15/14	917	76.1	20.8	0	4.8	9.92	.....	970	Green day
2/16/14	3,467	181.9	61.6	0	16.2	14.96	57.35	1,130	Green day
2/17/14	3,464	180.1	60.7	Trace	16.3	12.89	57.75	1,000	
2/18/14	3,421	175.9	60.1	13.20	16.1	14.74	58.88	1,650	
2/19/14	3,361	170.2	59.7	9.10	15.9	14.01	58.45	1,320	
2/20/14	3,469	181.1	59.7	13.70	16.1	16.08	58.24	1,600	

TABLE 5.—Felix K.: Clinical Data—(*Continued*)

Date	Total Calories	Fat, Gm.	Carbo., Gm. in Food	Glucose, Gm. in Urine	N in Food, Gm.	N in Urine, Gm.	Body Weight, Kg.	Urine Volume, c.c.	Remarks
2/21/14	3,347	171.2	59.5	5.88	15.0	11.10	58.89	1,310	
2/22/14	3,396	173.9	61.2	Traces	15.7	10.70	.....	1,460	
2/23/14	3,329	176.7	60.4	Traces	16.0	11.54	59.02	1,760	
2/24/14	3,318	174.8	38.6	Traces	14.7	11.45	59.17	1,405	Bread every two hours
2/25/14	3,460	181.3	58.3	Traces	16.0	12.10	.....	1,080	
2/26/14	920	76.6	20.6	0	4.8	9.09	58.60	1,110	
2/27/14	3,622	174.8	12.1	0	14.6	15.08	.....	1,480	
2/28/14	3,254	181.8	13 4	0	15.9	12.78	59.00	1,300	
3/ 1/14	3,494	218.4	38.2	0	14.4	15.08	.....	1,900	
3/ 2/14	3,341	177.6	39.6	0	15.6	15.60	59.16	2,120	
3/ 3/14	3,336	177.7	38.4	0	15.6	13.79	58.87	1,540	
3/ 4/14	3,375	177.6	47.2	0	15.8	12.72	59.51	1,400	
3/ 5/14	3,400	178.4	50.3	0	16.0	12.89	60.08	1,540	
3/ 6/14	3,486	179.6	65.0	0	16.5	12.69	60.07	1,440	
3/13/14	3,360	178.5	58.5	5.75	15.2	15.20	59.52	1,650	Oatmeal every two hours
3/14/14	943	78.4	20.8	0	5.0	10.87	59.37	1,400	Green day
3/15/14	927	77.1	20.8	0	4.8	5.77	59.22	870	Green day
3/16/14	2,007	112.0	178.0	24.39	9.1	10.31	.....	1,580	Bread day
3/17/14	2,013	112.6	178.0	27.03	9.2	8.85	58.81	1,390	Bread day
3/18/14	2,057	116.0	178.0	37.38	9.6	8.34	.....	1,786	Bread day
3/19/14	942	78.1	20.8	0	5.0	6.48	58.42	930	Green day
3/20/14	946	78.7	21.2	0	4.8	7.88	.....	1,877	Green day
3/21/14	3,388	173.1	61.4	0	15.6	11.98	.....	2,130	
3/22/14	3,359	173.4	58.3	15.86	14.9	10.31	.....	1,250	
3/23/14	3,164	199.5	66.7	Trace	15.0	11.04	.....	1,820	

The vegetables were increased until on July 30 he was taking 70.5 gm. carbohydrate, without glycosuria. Protein and fat were then slowly added, and an adequate diet attained without difficulty. Patient is a gourmand, and in September he was allowed to bring back his old symptoms by excess of fat in the diet, as an object-lesson. Two days' fasting stopped this glycosuria and suitable diet was resumed. In the latter part of October the average daily diet was approximately 114 gm. protein, 120 gm. carbohydrate, and from 2,600 to 2,900 calories. Calorimeter experiments were performed on October 30 and 31 and November 5. Patient was discharged on Nov. 9, 1915, weighing 61.2 kg. He has done his usual work since, with only an occasional temporary glycosuria after eating too much.

Case 5.—Felix K. (mild diabetes), clerk, 47 years old, born in Ireland. As a young man the patient had pneumonia, urethritis, and about four years ago an attack of malaria. He was a heavy drinker of beer and whisky up to five months ago. Lately he has taken but little alcohol. About one year ago he first noticed a loss of weight, with polyuria and weakness. Since then he has lost from 40 to 50 pounds. On admission to Bellevue, Oct. 28, 1913, he

was so weak that he could hardly walk upstairs. He is an emaciated man of medium stature. The lungs are emphysematous. There is slight exophthalmos, but no enlargement of the thyroid gland. Wassermann reaction + +; hemoglobin 98 per cent.; leukocytes 9,500; blood pressure: systolic 110, diastolic 75. His urine contained 61 gm. of glucose, 2.14 gm. ammonia, and small amounts of betaoxybutyric acid. The patient was in the general ward and it was difficult to control his diet. He was discharged on November 25, and on January 13 was readmitted, this time to the metabolism ward. Weight January 16, 56.5 kg. On a restricted diet his carbohydrate tolerance improved and his weight and strength increased rapidly (see Table 5). He was discharged March 24, 1914, in excellent condition. Since then he has reported from time to time, feeling perfectly well and strong, but showing sugar in the urine when he departs from his diet.

Case 6.—John O'C. (mild diabetes, morphinism), clerk, aged 32. His father was an alcoholic. At the age of 15 the patient had typhoid, and he has suffered from "pleurisy" eight times in the past few years. At the age of 16 he began to smoke opium, later taking to hypodermic injections of the drug, and one year ago he added cocain in increasing doses. Before admission he was taking 80 grains of cocain and 22 of morphin a day. This is his first attempt at breaking the habit. About two years ago he noticed polyuria and polydipsia and his doctor found sugar in the urine. He did not follow treatment and lost weight rapidly. He was very constipated, and so weak that he could hardly walk. Admitted to Bellevue Hospital March 13, weight March 24, 31.3 kg., height 163 cm. He was found to be nothing but skin and bones, toothless, with bent figure and ratlike, pathetic face. His whole body was covered with abscesses and scars of infections from hypodermic injections. There was a small ulcer on the sole of each foot. His pulse was very small, the beat normal, his tongue fissured, glassy and moderately red.

On a restricted diet the patient improved slowly and the glycosuria and acidosis cleared up (Table 6). He grew stronger but it was almost impossible to increase his weight without causing glycosuria. It was necessary to give him a grain of morphin every four hours. His systolic blood pressure varied between 104 and 125. On May 1, 1915, he was discharged and sent to a sanitarium, where he stayed a short time, then went back to his old habits and died a few months later.

SUMMARY AND COMMENT

1. *The Oatmeal Treatment.*—The mildly diabetic patient, Felix K., on a regulated diet containing about 60 gm. carbohydrate daily, showed a constantly positive carbohydrate balance and maintained his weight and well-being. February 10 and 11 were "green" days. Then from February 12 to 14, inclusive, 200 gm. oatmeal were given daily in the usual manner; then followed, Februry 15 to 16, two more "green" days. For comparison, beginning March 14, the same program was instituted, using bread instead of oatmeal, namely, first two "green" days, then March 16 to 18, inclusive, 265 gm. bread daily, equivalent in carbohydrate to the previous oatmeal, with fat, protein and calories also corresponding to the oatmeal period; then March 19 and 20 two more "green" days. Comparison was also made in a different manner, as follows: On February 24 he was given 18 gm. bread and 9 gm. butter every two hours, and on March 13 was given the equivalent carbohydrate in the form of 13.6 gm. oatmeal with 9 gm. butter every two hours.

TABLE 6.—JOHN O'C.:

Date	Food					
	Total Calories	Protein, Gm.	Fat, Gm.	Carbo., Gm.	Alcohol, Gm.	Food, N, Gm.
March 24-25	2,333	66.1	184.2	85.7	.....	10.57
March 25-26	1,842	81.1	131.2	70.4	.....	12.97
March 26-27	2,095	69.0	160.9	77.0	.....	11.04
March 27-28	2,021	79.4	147.3	84.2	.....	12.70
March 28-29	2,410	82.1	185.9	83.9	.....	13.13
March 29-30	2,508	82.1	195.9	85.2	.....	13.13
March 30-31	2,610	106.6	186.6	87.3	11.47	17.06
March 31-April 1	2,279	87.5	164.3	56.6	22.94	14.00
April 1- 2	2,488	88.7	183.7	62.4	22.94	14.19
April 2- 3	1,999	69.6	137.8	43.2	22.94	11.13
April 3- 4	294	0	0	0	42.00	0
April 4- 5	1,378	35.7	90.6	16.6	45.90	5.71
April 5- 6	1,941	44.1	126.5	142.5	.....	7.05
April 6- 7	1,594	47.0	87.8	142.5	.....	7.52
April 7- 8	1,753	47.0	104.8	142.5	.....	7.52
April 8- 9	2,148	57.2	194.3	25.9	.....	9.15
April 9-10	1,489	39.8	132.0	23.9	.....	6.36
April 10-11	1,783	48.1	154.4	36.6	.....	7.70
April 11-12	2,282	71.3	193.2	47.1	.....	11.41
April 12-13	2,435	76.0	200.7	61.6	.....	12.16
April 13-14	2,321	77.9	199.2	36.5	.....	12.46
April 14-15	2,178	70.6	187.6	35.0	.....	11.29
April 15-16	1,723	28.9	145.6	28.5	89.10	4.62
April 16-17	1,784	43.7	144.8	23.8	22.94	4.62
April 17-18	1,600	34.4	114.4	25.3	42.00	5.50
April 18-19	1,748	31.0	128.5	25.5	45.90	4.96
April 19-20	1,579	41.4	110.2	41.5	30.59	8.62
April 20-21	1,919	49.6	152.8	32.8	22.94	7.93
April 21-22	1,854	49.2	148.0	28.2	22.94	7.87
April 22-23	1,952	77.3	140.3	41.4	22.94	12.37
April 23-24	2,063	100.9	142.2	40.8	22.94	16.14
April 24-25	1,679	67.6	115.2	41.8	22.94	10.82
April 25-26	385	16.8	34.0	.....	.....	2.69
April 26-27	1,761	99.0	133.0	28.9	.....	15.84
April 27-28	737	25.3	60.6	16.7	.....	4.05
April 28-29	1,652	47.5	93.4	143.6	.....	7.60
April 29-30	1,674	47.0	96.3	142.5	.....	7.52
April 30-May 1	1,652	47.5	93.4	143.6	.....	7.60

Urine							Body Weight Kg.
Urine N, Gm.	Excreta N, Gm.§	N Balance, Gm.	Urine Glucose, Gm.	Urine NH_3, Gm.	Diacetic Acid	Urine Volume, c.c.	
13.34	14.40	—3.92	78.1	....	....	1,395	31.25
12.72	14.02	—1.05	55.7	1.70	Small amount	1,130	31.94
.....	.....	.....	....	....	....	.....	32.16
9.53* / 2.93†	11.20	+1.50	39.4	....	....	900	32.61
10.09	11.40	+1.73	43.7	....	....	1,480	33.80
9.92	11.23	+1.90	70.9	2.04	++	2,310	33.88
9.25	10.95	+6.11	53.3	1.80	+	2,000	33.63
10.54	11.94	+2.06	40.6	2.18	+++	1,550	33.14
9.53	10.95	+3.24	33.4	1.96	++	1,125	32.89
9.25	10.36	+0.97	23.6	1.96	+	920	32.89
6.02	.....	.....	+++	0.67	0	500	32.11
6.81	7.38	—1.67	0	0.26	0	735	32.69
8.41	9.12	—2.09	20.7	0.41	0	1,280	.....
6.44	7.19	+0.33	40.6	0.41	....	3,875	34.81
4.51	5.35	+2.17	29.7	0.75	0	2,900	32.71
5.76	6.68	+2.47	Heavy trace	0.57	0	1,490	32.26
6.72	7.36	—1.00	0	0.61	0	2,670	32.52
7.31	8.09	—0.39	0	0.39	....	1,620	31.79
6.22	7.36	+4.05	0	0.49	0	1,400	.....
8.28	9.50	+2.66	11.8	0.96	0	2,570	32.38
6.73	7.98	+4.48	7.2	0.82	Slight trace	1,440	31.79
8.99	10.12	+1.17	11.4	1.12	+	2,240	32.46
5.55	6.01	—1.39	2.6	0.79	Trace	1,200	32.52
5.04	5.74	+1.25	Slight trace	0.76	Heavy trace	1,880	32.12
5.04	5.59	—0.09	....	....	....	2,500	.....
5.37	5.87	—0.91	....	....	....	1,925	32.05
6.22	7.08	+1.54	0	....	0	1,820	31.61
5.80	6.59	+1.34	....	....	....	1,840	32.35
5.39	6.18	+1.69	0	0.51	0	1,940	32.52
6.35	7.59	+4.78	0	0.47	0	2,000	32.25
9.83	11.44	+4.70	0	0.59	0	1,725	32.45
9.18	10.26	+0.56	4.8	....	0	825	32.44
6.37	6.64	—3.95	0	....	Very heavy trace	600	.....
11.43	13.01	+2.79	0	0.98	Heavy trace	960	31.04
9.30	9.71	—5.66	0	0.93	Slight trace	660	31.88
8.58	9.34	—1.74	15.9	1.04	Trace	1,105	31.43
6.48	7.23	+0.29	21.2	1.14	0	1,960	32.46
6.39	7.15	+0.45	23.1	1.17	0	1,825	32.45

* 23 hours. † 24 hours. § Urine N = 10 per cent. of Food N.

TABLE 7.—DATA OF—

Subject, Date, Weight, Surface Area Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Gerald S.	Prelim.	11:15	.....	.....	.....	.....	.....	.....	.....
11/9/14	1	12:15	15.94	16.17	0.717	20.22	0.561	52.19	43.97
42.15 Kg.	2	1:15	16.32	16.39	0.724	20.85	0.561	52.94	17.51
1.44 Sq. M.	3	2:15	16.34	16.58	0.717	20.96	0.561	53.55	51.11
Gerald S.§	Prelim.	11:15	.....	.....	.....	.....	.....	.....	.....
11/12/14	1	12:15	16.27	15.87	0.746§	22.44	0.307	52.15	49.24
40.15 kg.	2	1:15	16.95	17.45	0.706	23.81	0.307	56.71	54.44
1.41 Sq. M.	3	2:15	15.50	17.61	0.640	24.32	0.307	57.19	56.77
Gerald S.	Prelim.	10:24	.....	.....	.....	.....	.....	.....	.....
11/14/14	1	11:24	15.41	16.00	0.700	17.66	0.441	51.87	45.12
38.97 Kg.	2	12:24	15.35	15.84	0.705	18.65	0.441	51.35	49.85
1.40 Sq. M.	3	1:24	15.30	15.87	0.701	18.71	0.441	51.45	51.61
Gerald S.	Prelim.	11:22	.....	.....	.....	.....	.....	.....	.....
11/16/14	1	12:22	13.85	14.29	0.705	29.82	0.347	46.34	43.67
38.77 Kg.	2	1:22	14.59	14.84	0.715	26.65	0.347	48.18	49.69
1.40 Sq. M.	3	2:22	15.27	14.73	0.754	24.96	0.347	48.25	50.03
	4	3:22	14.53	15.57	0.680	23.60	0.347	50.55	49.39
Gerald S.	Prelim.	11:06	.....	.....	.....	.....	.....	.....	.....
11/18/14	1	12:06	12.17	12.41	0.713	13.42	0.247	40.40	34.51
38.74 Kg.	2	1:06	13.00	13.45	0.718	13.97	0.247	42.82	38.89
1.40 Sq. M.	3	2:06	14.19	13.43	0.769	14.61	0.247	44.27	41.69
	4	3:06	13.76	14.44	0.693	14.75	0.247	47.06	44.15
	5	4.06	13.45	13.06	0.685	14.47	0.247	42.85	40.50
Gerald S.	Prelim.	11:06	.....	.....	.....	.....	.....	.....	.....
11/20/14	1	12:06	13.37	12.50	0.778	17.60	0.22	41.60	39.42
38.74 Kg.	2	1:06	12.20	12.82	0.692	16.68	0.22	42.06	41.23
1.40 Sq. M.	3	2:06	12.28	12.13	0.736	16.19	0.22	39.92	41.02
	4	3:06	15.43	14.29	0.785	16.43	0.22	47.67	43.08
Gerald S.	Prelim.	11:15	.....	.....	.....	.....	.....	.....	.....
11/23/14	1	12:15	13.02	13.54	0.699	12.99	0.232	44.14	38.70
42.84 Kg.	2	1:15	13.64	12.61	0.786	13.10	0.232	41.76	38.23
1.45 Sq. M.	3	2:15	12.56	13.11	0.697	14.15	0.232	42.72	42.79
Gerald S.	Prelim.	11:06	.....	.....	.....	.....	.....	.....	.....
11/24/14	1	12:06	12.80	11.70	0.796	13.09	0.237	38.79	36.04
44.00 Kg.	2	1:06	13.56	13.94	0.707	13.95	0.237	45.44	39.79
1.46 Sq. M.	3	2:06	13.22	12.51	0.768	13.69	0.237	41.23	38.55
	4	3:06	12.10	11.85	0.742	14.13	0.237	38.78	38.96

§ Calculations in summary based on total O_2 and CO_2 for 3 hours.

—Calorimeter Experiments

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. Meeh	
.....	36.28	..	....	.....	....	....	....	....	.....	Basal; D:N assumed to be 1.53 on basis of R.Q. Very quiet
55.18	36.61	71	4	0.704	22.4	77.6	0	1.24	35.01	
55.57	36.85	76	8	0.714	22.1	77.9	0	1.26	35.51	
51.13	36.86	77	4	0.705	21.8	78.2	0	1.27	35.92	
.....	37.14	..	....	.....	....	.	. ..	....	.....	Second day of fast; basal
52.23	37.24	99	7.2	0.755	8.0	75.1	16.9	1.30	36.11	Asleep 50 min.
54.77	37.26	102	10.5	0.711	7.4	91.3	1.3	1.41	39.27	Asleep 40 min.
55.45	37.23	99	2.0	0.639*	7.3	92.7	0	1.42	39.61	Asleep 30 min.
.....	36.54	..	....	.....	....	....	.	....	.....	Fourth day of fast; basal
49.33	36.68	81	7.8	0.68*	19.4	80.6	0	1.33	36.66	Asleep
41.13	36.42	..	7.6	0.69*	19.6	80.4	0	1.32	36.29	Asleep
51.95	36.44	79	12.0	0.68*	19.5	80.5	0	1.32	36.36	Asleep 45 min.
.....	36.16	..	....	.....	....	....	....	....	.....	Basal
40.14	36.03	..	9.0—	0.695	15.5	84.5	0	1.20	32.86	Asleep
53.54	36.16	..	13.0—	0.708	14.8	84.0	1.2	1.24	34.17	Asleep
48.88	36.08	70	15.8—	0.754	14.8	72.4	12.8	1.25	34.22	Drank 20 c.c. whisky at 1:27 p. m.
49.10	36.08	..	17.0—	0.665	14.2	85.8	0	1.30	35.85	Asleep
.....	35.76	..	....	.....	....	....	....	....	. ...	Basal
26.05	35.51	..	4	0.697	15.5	84.5	0	1.04	28.65	Asleep
39.33	35.52	..	4	0.705	14.6	85.4	0	1.11	30.57	Basal, asleep
53.62	35.84	..	12	0.764	14.1	70.1	15.8	1.14	31.40	Drank 20 c.c. whisky at 1:08 p. m. Asleep 40 min.
53.62	36.14	..	13	0.676	13.2	86.8	0	1.22	33.38	Asleep 55 min.
34.91	35.97	..	7	0.740	14.6	75.5	9.9	1.11	30.39	Asleep 55 min.
.....	35.88	..	....	.....	....	....	....	....	.....	Whisky, 20 c.c. at 11:08 a. m.
37.70	35.78	..	6	0.773	14.7	66.7	18.6	1.07	29.50	Dozed
40.06	35.75	..	4	0.673	14.5	85.5	0	1.09	29.83	Dozed
42.74	35.81	..	3	0.724	15.3	79.2	5.5	1.03	28.31	Dozed
46.44	35.92	..	19	0.782	12.8	65.2	22.0	1.23	33.04	Restless
.....	35.99	..	....	.....	....	....	....	. .	.....	Basal
37.09	35.95	47	8	0.681	13.9	86.1	0	1.03	29.29	Asleep 30 min
43.05	36.04	..	11	0.783	14.7	63.8	21.5	1.00	27.71	Awake
34.37	35.81	52	14	0.678	14.4	85.6	0	1.00	28.35	Awake
.....	35.85	..	....	.....	....	....	....	. .	.....	Basal
36.30	35.85	52	4.0	0.794	16.2	59.9	23.9	0.90	25.29	Quiet
41.16	35.90	51	5.5	0.691	13.8	86.2	0	1.03	29.62	Quiet
40.63	35.96	..	5.0	0.762	15.2	69.2	15.6	0.94	26.88	Drank 1 drop of water
31.21	35.75	50	2.2	0.730	16.2	76.9	6.9	0.90	25.28	Quiet

* R. Q. assumed as 0.707 for calculations.

TABLE 7.—Data of Calorimeter—

Subject, Date, Weight, Surface Area Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Gerald S.	Prelim.	11:15	.....	.....	.....	.....	.....	.....	.....
11/25/14									
44.04 Kg.	1	12:15	12.72	12.20	0.753	14.98	0.235	40.32	36.55
1.46 Sq. M.	2	1:15	13.21	12.40	0.775	15.14	0.235	40.96	37.95
	3	2:15	13.03	12.29	0.771	15.61	0.235	40.59	38.83
	4	3:15	11.87	12.68	0.680	15.97	0.235	41.31	40.58
Gerald S.	Prelim.	11:27	.....	.....	.....	.....	.....	.....	.....
11/30/14									
44.27 Kg.	1	12:27	14.38	14.09	0.742	21.28	0.228	46.18	39.28
1.47 Sq. M.	2	1:27	14.07	13.45	0.760	20.78	0.228	44.27	42.66
	3	2:27	14.80	14.13	0.762	20.24	0.228	46.63	41.57
	4	3:27	14.36	14.27	0.732	20.30	0.228	46.67	45.91
Gerald S.	Prelim.	11:12	.....	.....	.....	.....	.....	.....	.....
12/2/14									
44.76 Kg.	1	12:12	15.59	15.21	0.745	24.90	0.208	50.03	42.79
1.47 Sq. M.	2	1:12	13.27	12.57	0.768	22.51	0.208	41.48	42.54
	3	2:12	16.92	16.38	0.751	24.10	0.208	54.02	50.44
	4	3:12	14.97	13.99	0.779	23.39	0.208	46.31	44.84
Gerald S.	Prelim.	11:09	.....	.....	.....	.....	.....	.....	.....
12/4/14									
43.94 Kg.	1	12:09	15.81	14.79	0.778	19.79	0.204	48.99	41.38
1.46 Sq. M.	2	1:09	16.43	.....	.....	19.61	0.204	50.91*	44.13
	3	2:09	13.93	13.34	0.759	18.19	0.204	43.95	42.59
	4	3:09	14.85	14.53	0.743	18.78	0.204	47.68	45.98
Gerald S.	Prelim.	11:10	.....	.....	.....	.....	.....	.....	.....
12/7/14									
42.58 Kg.	1	12:10	14.77	13.78	0.780	18.90	0.216	45.69	40.83
1.45 Sq. M.	2	1:10	15.08	15.19	0.722	19.31	0.216	49.59	45.09
	3	2:10	13.93	13.15	0.770	18.21	0.216	43.48	44.55
	4	3:10	14.40	13.69	0.765	18.41	0.216	45.18	45.10
William G.	Prelim.	11:20	.....	.....	.....	.....	.....	.....	.....
1/11/15									
43.28 Kg	1	12:20	13.39	12.62	0.772	16.14	0.170	41.83	40.94
1.53 Sq. M.	2	1:20	14.30	13.84	0.750	16.38	0.170	45.67	43.05
	3	2:20	13.74	14.26	0.701	16.45	0.170	46.60	47.13
William G.	Prelim.	11:07	.....	.....	.....	.....	.....	.....	.....
1/15/15									
43.84 Kg.	1	12:07	15.11	14.72	0.747	24.83	0.291	48.34	42.16
1.54 Sq. M.	2	1:07	14.49	15.73	0.670	24.11	0.291	51.03	47.43
	3	2:07	14.21	14.66	0.705	24.30	0.291	47.56	49.04
William G.	Prelim.	11:12	.....	.....	.....	.....	.....	.....	.....
1/22/15									
37.87 Kg.	1	12:12	15.29	16.38	0.679	17.02	0.382	53.05	49.18
1.46 Sq. M.	2	1:12	14.80	15.66	0.688	17.32	0.382	50.69	48.96
	3	2:12	15.46	15.87	0.708	18.36	0.382	51.42	51.88

* Calc., from CO_2, R. Q. assumed 0.778.

—EXPERIMENTS—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. Mech	
.....	36.12	..	....	.....	....	....	....	....	.....	Basal
33.16	36.03	48	3.5	0.743	15.4	74.8	9.8	0.97	26.27	Dozed
37.01	36.01	..	2.7	0.769	15.2	66.3	18.5	0.93	26.68	Dozed
37.25	35.95	..	0.5	0.765	15.4	66.2	18.4	0.92	26.44	At 1:17 drank 20 c.c. whisky from tube
33.07	35.75	51	2.8	0.659	15.1	84.9	0	0.94	26.91	Dozed
.....	36.31	..	....	.....	....	....	....	....	.....	Basal
37.96	36.28	58	4.7	0.732	13.1	79.8	7.1	0.86	24.61	Quiet
46.86	36.40	53	8.5	0.753	13.7	73.4	12.9	1.00	28.73	Quiet
40.21	36.32	56	16.5	0.755	13.0	71.0	16.0	1.05	30.26	Drank 170 c.c. water at 1:28 p. m.
44.22	36.28	52	9.4	0.720	13.0	82.8	4.2	1.05	30.29	Quiet
.....	36.66	..	....	.....	....	....	....	....	.....	Basal
39.51	36.58	56	5.1	0.738	11.1	78.6	10.3	1.12	32.24	Quiet
37.03	36.44	55	1.1	0.762	13.3	70.8	15.9	0.93	26.73	Quiet
52.36	36.50	58	15.4	0.745	10.2	76.3	13.5	1.21	34.81	Exercised 10 min.
49.81	36.64	53	5.8	0.774	11.9	68.9	19.2	1.04	29.84	Quiet
.....	36.08									
48.84	36.29	58	2.6	0.773	11.0	69.6	19.4	1.12	31.96	Exercised 10 min.
51.94	36.51	..	5.7	.....	....	....	....	....	.....	Exercised 10 min.
43.85	36.55	59	2.9	0.752	12.3	74.6	13.2	1.00	28.67	Quiet
43.22	36.48	..	2.8	0.734	11.3	81.4	7.3	1.09	31.11	Quiet
.....	36.46	..	....	.....	....	....	....	....	.....	Basal
43.09	36.53	55	21.2	0.776	12.5	65.4	22.0	1.07	30.42	Quiet
48.78	36.64	56	19.4	0.711	11.6	87.2	1.2	1.17	33.02	Quiet
43.58	36.61	54	25.4	0.765	13.2	67.9	18.9	1.02	28.95	Quiet
44.95	36.61	56	23.6	0.759	12.7	71.3	16.1	1.06	30.08	Quiet
.....	36.76	..	....	.....	....	....	....	....	.....	Basal
42.16	36.80	65?	2.9	0.767	10.8	69.7	19.5	0.97	27.57	Asleep
38.53	36.68	65?	10.7	0.743	9.8	79.7	10.5	1.10	30.10	Awake, quiet
48.46	36.72	53	7.4	0.689§	9.7	90.3	0	1.10	30.72	Awake, quiet
.....	36.75	..	....	.....	....	....	....	....	.....	Basal, D:N 3.81 †
37.58	36.63	64	7.0	0.757	7.9	75.2	16.9	1.10	31.57	Asleep
47.22	36.63	64	9.6	0.673	7.4	92.6	0	1.16	33.33	Asleep
52.84	36.74	62	9.6	0.712	8.0	90.7	1.3	1.10	31.06	Asleep
.....	36.98	..	....	.....	....	....	....	....	.....	Basal, D:N 3.12
46.13	36.89	64	8.5	0.679	10.8	89.2	0	1.40	38.19	Dozed
46.55	36.82	64	2.2	0.689	11.3	88.7	0	1.34	36.50	Quiet
52.30	36.84	63	6.5	0.713	11.1	88.9	0	1.40	37.02	Quiet

† D:N assumed as 3.65 for calculations.
§ R. Q. assumed as 0.707 for calculations.

TABLE 7.—Data of Calorimeter—

Subject, Date, Weight, Surface Area Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Joseph U.	Prelim.	11:15	.....	.....	.....	.....	.....	.....	.....
2 1/15									
40.14 Kg.	1	12:15	11.56	11.45	0.734	18.41	0.188	37.45	42.09
1.45 Sq. M.									
	2	1:15	11.57	11.26	0.747	17.79	0.188	36.99	42.18
	3	2:15	11.39	11.07	0.748	16.90	0.188	36.36	40.80
Edward M.	Prelim.	11:15	.....	.....	.....	.....	.....	.....	.....
10/30/14									
60.59 Kg.	1	12:15	20.58	18.19	0.823	25.35	0.391	60.77	62.97
	2	1:15	20.88	19.29	0.787	26.61	0.391	63.80	66.38
Edward M.	Prelim.	11:33	.....	.....	.....	.....	.....	.....	.....
10/31/14									
60.92 Kg.	1	12:33	21.62	19.88	0.791	23.02	.....	66.23	54.37
	2	1:33	21.04	20.01	0.765	23.56	.....	66.29	61.79
	3	2:33	22.64	20.27	0.812	24.87	.....	67.89	66.77
Edward M.	Prelim.	11:17	.....	.....	.....	.....	.....	.....	.....
11/5/14									
62.16 Kg.	1	12:17	24.93	23.98	0.756	28.04	0.594	78.49	67.80
	2	1:17	25.27	24.55	0.748	28.96	0.594	80.21	76.64
	3	2:17	24.33	23.40	0.756	28.88	0.594	76.57	79.61
Felix K.	Prelim.	11:15	.....	.....	.....	.....	.....	.....	.....
2/11/14									
57.56 Kg.	1	12:15	20.18	19.36	0.758	22.51	0.325	63.74	66.09
	2*	2:15	44.10	43.06	0.745	44.78	0.650	141.40	140.20
Felix K.	Prelim.	12:05	.....	.....	.....	.....	.....	.....	.....
2/12/14									
57.84 Kg.	1	1:05	25.25	24.14	0.761	25.89	0.607	79.14	71.51
	2	2:05	26.63	24.85	0.779	31.64	0.607	81.91	89.43
	3	3:05	24.91	23.94	0.757	41.94	0.607	78.40	96.59
Felix K.	Prelim.	11:08	.....	.....	.....	.....	.....	.....	.....
2/14/14									
57.80 Kg.	1	12:08	25.79	23.83	0.787	23.97	0.481	78.91	75.60
	2	1:08	24.78	21.55	0.836	26.91	0.481	72.18	78.93
	3	2:08	24.53	21.55	0.828	27.69	0.481	72.03	80.44
Felix K.	Prelim.	12:20	.....	.....	.....	.....	.....	.....	.....
2/24/14									
58.70 Kg.	1	1:20	22.67	21.44	0.769	18.70	0.362	70.96	78.23
	2	2:20	22.61	20.08	0.819	19.99	0.362	67.13	77.64
	3	3:20	22.89	21.19	0.786	20.82	9.362	70.27	76.74
Felix K.	Prelim.	11:02	.....	.....	.....	.....	.....	.....	.....
2/26/14									
58.57 Kg.	1	12:02	21.00	.....	.....	18.95	0.326	.....	75.40
	2	1:02	21.76	20.52	0.771	20.88	0.326	67.66	76.05
	3	2:02	21.64	19.60	0.803	20.55	0.326	65.30	74.30
Felix K.	Prelim.	11:50	.....	.....	.....	.....	.....	.....	.....
3/13/14									
59.29 Kg	1	12:50	21.60	20.44	0.768	21.60	0.789	66.62	74.07
	2	1:50	21.63	20.31	0.774	20.94	0.789	66.29	72.80
	3	2:50	22.03	20.03	0.800	21.42	0.789	65.80	73.09

—EXPERIMENTS—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. Meeh	
.....	36.56	..	....	....	....	....	....	....	.....	Basal
36.33	36.39	72	3.0	0.723	13.3	82.6	4.1	0.93	25.95	Very quiet
40.52	36.35	72	2.5	0.738	13.5	76.5	10.0	0.92	25.63	Very quiet
30.62	36.05	73	12.0	0.739	13.7	76.3	10.0	0.91	25.20	Quiet
.....	37.31	..	....	....	....	....	....	....	.....	Basal
55.09	37.16	52	34	0.827	17.1	48.0	35.0	1.00	32.74	Restless
55.99	36.96	53	21	0.784	16.3	70.2	21.1	1.05	34.37	Quiet
.....	36.76	..	....	.....	....	....	....	....	.....	97 gm. olive oil at 10:03 a. m.
58.10	36.84	64	27	.....	....	....	....	1.09	34.74	Quiet
65.49	36.92	60	20	.....	....	....	....	1.09	34.78	Quiet
66.45	36.92	55	46	.....	...	....	....	1.11	35.62	Restless
.....	.....	..	....	.....	....	....	....	1.10	35.00	Urine lost
.....	36.94	..	....	.....	....	....	....	....	.....	Breakfast at 7 96 gm. olive oil at 9:17 a. m.
69.54	36.98	71	....	0.743	20.0	70.7	9.3	1.26	40.63	Quiet
78.39	37.02	60	....	0.734	19.6	73.8	6.6	1.29	41.52	Quiet
78.80	37.01	67	....	0.743	20.6	70.2	9.2	1.23	39.63	Quiet
.....	37.18	..	....	.....	....	....	....	....	.....	Basal
49.49	36.84	..	5.6	0.751	14	73	13	1.11	34.74	Asleep
148.21	37.06	69	38.5	0.736	12	79	9	1.23	38.53	Fairly quiet
.....	37.53	..	....	.....	....	....	....	....	.....	At 10:45 to 10:52: oatmeal, 125; butter, 15; protein, 18.8; fat, 19.8; carb., 89.1
64.43	37.39	80	6.8	0.749	20	68	12	1.37	42.99	
89.21	37.42	79	24.4	0.773	20	62	18	1.42	44.49	
88.69	37.28	71	26.0	0.744	21	69	10	1.35	42.59	
.....	37.21	..	....	.....	....	....	....	....	.....	At 9:45 to 9:53: oatmeal, 125; butter, 15
70.91	37.12	76	12.5	0.783	16	62	22	1.37	42.89	
78.10	37.11	..	21.9	0.843	18	44	38	1.25	39.23	
80.50	37.17	85	13.0	0.833	18	47	35	1.25	39.15	
.....	37.19	..	....	.....	....	....	....	....	.....	Bread, 18; butter, 9, every 2 hrs., last taken at 11:37 a. m.
71.53	37.06	..	7.5	0.774	14	66	20	1.21	38.15	
74.35	37.00	69	8.3	0.822	14	52	34	1.14	36.09	
77.84	37.03	75	7.4	0.783	14	63	23	1.19	37.78	
.....	37.08	..	....	.....	....	....	.. .	....	. ...	Basal
72.11	37.02	72	6.8	.....	....	....	....	....	.....	Very quiet
73.10	37.06	..	7.9	0.769	13	68	19	1.15	36.44	Very quiet
74.45	37.07	75	10.0	0.802	13	59	28	1.12	35.16	Very quiet
.....	36.87	..	....	.....	....	....	....	....	.....	Oatmeal 13.6, butter 9, every 2 hrs., last taken at 11:07 a. m.; asleep 1st period and half of second
65.35	36.70	76	9.0	0.751	31	58	11	1.12	35.59	
72.95	36.71	76	7.2	0.760	32	55	13	1.12	35.41	
74.71	36.75	75	13.2	0.798	32	47	21	1.11	35.15	

TABLE 7.—Data of Calorimeter—

Subject, Date, Weight, Surface Area Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Felix K. 3/18 14	Prelim.	11:25	.....	.....	.....	.....	.....	.....	.....
58.38 Kg.	1	12:25	23.83	22.18	0.781	22.75	0.373	73.47	71.91
	2	1:25	24.44	21.90	0.812	25.72	0.373	73.12	79.87
	3	2:25	22.15	19.18	0.840	24.78	0.373	64.42	73.67
	4	3:25	22.07	19.81	0.810	24.28	0.373	66.04	74.31
Felix K. 3/20,14	Prelim.	12:00	.....	.....	.....	.....	.....	.....	.....
57.84 Kg.	1	1:00	18.79	17.54	0.779	18.15	0.338	57.97	60.50
	2	2:00	20.17	19.60	0.748	19.90	0.338	64.34	65.02
	3	3:00	20.25	18.92	0.778	20.94	0.338	62.58	64.95
John O'C. 4/28/15	Prelim.	11:34	.....	.....	.....	.....	.....	.....	.....
31.43 Kg. 1.20 Sq. M.	1	12:34	14.26	9.92	0.732	24.34	0.381	46.05	47.99
	2	1:34	15.07	9.45	0.812	24.86	0.381	44.74	48.82
John O'C. 4/30/15	Prelim.	11:46	.....	.....	.....	.....	.....	.....	.....
32.45 Kg. 1.22 Sq. M.	1	12:46	14.25	12.85	0.804	22.96	0.262	42.80	43.58
	2	1:46	14.87	14.14	0.765	26.25	0.262	46.63	50.53

Glycosuria: The urine always became promptly and completely sugar-free on "green" days. The total amount of glucose excreted during the oat period was 64.1 gm., during the bread period 88.8 gm. This difference is fully comparable to those in the literature upon which the claims of superiority of oatmeal have been based. But, as Blum pointed out, spontaneous fluctuations in diabetic glycosuria must be allowed for, even when all conditions are kept as uniform as possible, and a repetition of the same test sometimes gives a variation in the opposite direction. The more favorable carbohydrate balance in this instance speaks no more for oatmeal than the less favorable nitrogen balance during this same time speaks against oatmeal. This interpretation is supported by the results of the other test; for on the days when the carbohydrates were given in small divided doses it so happened that the glycosuria from bread was only a trace, while that from oatmeal amounted to 5.75 gm. A consistent difference in favor of oatmeal is therefore not present.

Respiration Experiments: This patient on February 12, while fasting in the morning after a "green" day of eggs, butter and green vegetables of the 5 per cent. class, derived from 10 to 13 per cent. of the calories from carbohydrate. On the first oatmeal day he derived 13

—EXPERIMENTS—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. Mech	
.....	37.16	..	....	.....	....	....	....	....	.....	At 9:45 to 10:06 a.m., bread 168, butter 15
63.34	36.99	67	11.3	0.777	13	66	21	1.12	39.67	
81.41	37.07	73	28.3	0.813	14	55	31	1.25	39.48	
69.51	37.01	71	22.2	0.847	15	44	41	1.10	34.78	
68.62	36.94	70	27.0	0.811	15	55	30	1.13	35.66	
.....	36.88	..	....	.....	....	....	....	....	....	Basal
51.32	36.65	59	10.6	0.774	15	65	20	1.00	31.51	Asleep 3[illegible] min.
66.74	36.80	60	15.1	0.739	14	76	10	1.11	34.97	Quiet
67.66	36.88	62	13.3	0.774	14	66	20	1.08	34.01	Quiet
.....	36.43	..	....	.....	....	....	....	....	.....	1st oatmeal day. Oatmeal 50, butter 10, at 6:30 a. m. and again at 9:34 a. m., restless 2d period
45.42	36.34	58?	16.1	0.711	21.9	77.0	1.1	1.47	37.56	
48.22	36.33	76?	22.8	0.814	22.6	50.0	27.4	1.42	36.49	
.....	36.32	..	....	.....	....	....	....	....	.....	3d oatmeal day. Same food as above
42.28	36.27	67	9.0	0.807	16.2	54.1	29.7	1.32	34.19	Quiet
46.71	36.15	72	18.0	0.757	14.9	69.4	15.7	1.44	37.25	Restless

per cent., and on the third oatmeal day 32 per cent. from carbohydrate. If the metabolism of carbohydrate continued at this rate of 32 per cent. throughout the day, he could have utilized about 145 gm. The positive carbohydrate balance on that day was 149 gm. On March 18, the third day on which he received the same amount of starch in the form of bread, he derived 31 per cent. of his calories from this source; he utilized about 130 gm., and the positive balance was 147 gm. He was able to derive 26 per cent. of his calories from carbohydrate after small divided meals of bread and butter, and as much as 24 per cent. while fasting on the morning after his usual diet, which just kept him sugar-free. After similar doses of oatmeal he derived only 15 per cent. from carbohydrate. The respiration experiments therefore show no significant difference between the starch of bread and that of oatmeal in this case.

The morphin addict, John O'C., with mild diabetes, gave exactly the same results, namely, on the first oatmeal day, April 28, 14 per cent. from carbohydrate, on the third day, April 30, 23 per cent. He was not tested with bread.

It is quite possible that the slightly lower combustion of carbohydrate indicated by the quotients on the first as compared with the

TABLE 8.—INDIRECT

Subject and Date	Character of Experiment	Calories per kg.	Average Calories per Hour		Per Sq. M., Linear
			Per Sq. M., Meeh	Per Cent. from Average Normal, 34.7	
Gerald S.					
11/ 9/14	Basal	1.26	35.6	+ 2	36.7
11/12/14	Basal, second day of fast	1.38	38.3	+11	39.1§
11/14/14	Basal, fourth day of fast	1.32	36.4	+ 5	36.4
11/16/14	Basal, sixth day of fast	1.22	33.5	- 3	33.9
	Two hours after whisky	1.28	35.0	2	35.4
11/18/14	Basal, eighth day of fast	1.08	29.5	—15	29.8
	Three hours after whisky	1.15	31.7	....	32.0
11/20/14	Four hours after whisky	1.11	30.2	....	30.7
11/23/14	Basal, fifth day of feeding	1.00	28.5	—18	29.6
11/24/14	Basal, sixth day of feeding	0.93	26.8	23	28.0
11/25/14	Basal, seventh day of feeding	0.92	26.5	—24	27.7
	Two hours after whisky	0.93	26.7	....	28.0
11/30/14	Basal (with water drinking)	0.99	28.5	—18	31.4
12/ 2/14	Basal	1.02	29.5	—15	31.0
	Basal with exercise	1.12	32.3	....	34.8
12/ 4/14	Exercise with basal	1.07	30.6	....	32.7
12/ 7/14	Basal	1.08	30.6	—12	31.8
William G.					
1/11/15	Basal	1.03	29.5	—15	29.3
1/15/15	Basal	1.12	32.0	— 8	31.9
1/22/15	Basal	1.37	37.2	+ 7	35.5
Joseph U.					
2/1/15	Basal	0.92	25.6	—26	25.4
Edward M.					
10/30/14	Basal	1.03	33.6	— 3	....
10/31/14	Two to five hours after 97 gm. olive oil	1.10	35.0	....	....
11/ 5/14	Two to five hours after 96 gm. olive oil following breakfast	1.29	40.9	+17	....
Felix K.					
2/11/14	Basal after 1 green day	1.19	37.3	+ 7	....
2/12/14	1¼ to 4¼ hours after 125 gm. oatmeal, 15 butter	1.38	43.4	....	....
2/14/14	1¼ to 4¼ hours after 125 gm. oatmeal, 15 butter; third oatmeal day	1.29	40.4	....	....
2/24/14	After 18 gm. bread and 9 butter every two hours	1.18	37.3	....	....
2/26/14	Basal	1.13	35.8	+ 3	....
3/13/14	After 13.6 oatmeal and 9 butter every two hours	1.12	35.4	....	....
3/18/14	1½ to 5½ hrs. after 16S bread and 15 butter, 3d bread day	1.18	37.4	....	....
3/20/14	Basal after one green day	1.06	33.5	— 4	....
John O'C.					
4/28/15	After 100 gm. oatmeal and 20 butter, first oatmeal day	1.45	37.0	(+ 7)	37.7
4/30/15	After same food, third oatmeal day	1.38	36.7	(+ 3)	36.7

* On account of respiratory quotient, dextrose-nitrogen ratio assumed to be 1.53 for purpose of calculation.
† Nonprotein respiratory quotient assumed 0.707 for calculations.

CALORIMETRY SUMMARY

Per Cent. from Average Normal 39.7	Average R. Q.	Average Non-protein R. Q.	Per Cent. Cal. from Carb.	Per Cent. Divergence of Direct from Indirect Cal.	Average Pulse	Remarks
— 8	0.719	0.707*	0	+ 2	75	Very quiet; D.-N. 1.53*
— 1	0.697	0.709§	0§	— 2§	100	Asleep; D.-N. 3.5
— 8	0.702	0.68 †	0	— 8	80	Asleep; D.-N. 1.0
—15	0.710	0.701	1	— 1	..	Asleep; D.-N. 1.55
....	0.717	0.710	6	— 1	70	Asleep; D.-N. 1.55
—25	0.716	0.701	0	—21	..	Asleep; D.-N. 0.33
....	0.737	0.727	6	+ 6	71	Awake; D.-N. 0.33
.. .	0.748	0.739	10	+ 1	61	Dozed
—26	0.727	0.712	2	—11	49	Awake
—29	0.753	0.744	10	— 9	51	Quiet
—30	0.764	0.756	14	—14	48	Dozed
....	0.726	0.712	1	—14	51	Dozed
—21	0.749	0.740	10	— 7	55	Quiet
—22	0.757	0.750	13	—16	56	Quiet
....	0.765	0.760	16	+ 2	56	Flexed arms 10 min.
....	0.760	0.753	13	— 2	59	Flexed arms 10 min. in first two periods
—20	0.759	0.753	15	— 2	55	Quiet
—26	0.741	0.732	7	— 4	61	Quiet
—20	0.707	0.714	0	— 6	63	Very quiet, dozed; D.-N. 3.8‡
—11	0.692†	0.693	0	— 7	64	Quiet; D.-N. 3.12
—36	0.743	0.733	8	— 3	72	Very quiet
....	0.805	0.806	28	—11	53	Fairly quiet
....	0.789	.....	....	— 5	59	Fairly quiet; urine lost
....	0.753	0.740	8	— 4	69	Quiet; breakfast at 7 a. m., Prot. 14, fat 204, Carb. 38
....	0.749	0.741	10	4	69	Fairly quiet
....	0.766	0.755	13	+ 1	77	Fairly quiet
....	0.817	0.820	32	+ 3	81	Fairly quiet
....	0.791	0.793	26	+ 7	72	Quiet
....	0.787	0.786	24	+11	74	Very quiet
....	0.781	0.770	15	+ 7	76	Asleep one half exper.
....	0.811	0.812	31	+ 2	70	Fairly quiet
....	0.768	0.762	13	+ 0	60	Quiet
(— 5)	0.772	0.763	14	+ 3	64	Fairly quiet
(— 8)	0.784	0.782	23	— 1	69	Fairly quiet
				Av. ± 5.5		

‡ D:N ratio assumed to be 3.65 for calculations.
§ Calculated from total O_2 and CO_2 for three hours.

third day of carbohydrate diet may indicate storage of glycogen after impoverishment on the preceding vegetable day, in harmony with the observations of Johansson and others on this point. The experiments fail to confirm Falta's conception of a striking difference in the manner of utilization of carbohydrate by diabetics on the first and third days of such a "cure." It would be desirable also to have information concerning the behavior of a normal subject under the same conditions, but such an experiment was not included in the present series.

Carbohydrate and water retention: The quantities of carbohydrate not accounted for by combustion are in all these experiments such as may easily be assumed to be stored as glycogen. The experiments are not of a character such as to throw light on the fate of carbohydrate under circumstances when, as Joslin[5] reckons, as much as 520 gm. may be retained and not accounted for by differences in the respiratory exchange. The fate of carbohydrate under these conditions must be regarded as not definitely settled. Glycogen storage is known to be commonly associated with water retention. Aside from the edema which authors have shown to be attributable to sodium chlorid and bicarbonate, the gain in weight of some diabetics during the oatmeal treatment may be related to the carbohydrate retention. It will be noted that the patient John O'C. actually gained about a kilogram in weight during the oatmeal period. On the other hand, Felix K., with a larger carbohydrate intake and apparent storage, gained no weight during his oatmeal period and lost a trifle during the bread period. This result therefore stands in marked contrast to the well-marked increase in weight which ordinarily occurs when a normal person changes from carbohydrate-poor to carbohydrate-rich diet.

2. *The Dextrose-Nitrogen Ratio.*—The cases of interest in this connection are those of William G., Gerald S., and that of Cyril K., which was described by Geyelin and DuBois; also another case more recently observed, a description of which will be published shortly by Gephart, Aub and DuBois.

William G., as previously stated, at first upon admission to the Presbyterian and Rockefeller Hospitals was found to show a dextrose-nitrogen ratio of approximately 3, with a strongly negative nitrogen balance. Table 4 contains his record six months later, during a period of feeding in the attempt to improve his strength. Starting with sugar-free urine on January 11, increase of protein and fat in the diet produced prompt glycosuria, with dextrose-nitrogen ratios higher than before. At least on January 15 and 20 the ratio was that of "total" diabetes. The actual quantities of both sugar and nitrogen excreted were less than in the former period when the ratios were smaller; and the nitrogen deficit was less although the diet was lower than before in both protein and calories. The clinical condition changed so rapidly

for the worse and the patient on January 22 was so ill and drowsy that it was necessary to resort to fasting to avert coma.

In Gerald S. the dextrose-nitrogen ratio was confused by the presence of carbohydrate in the diet until November 11. On this day no food was taken except 50 c.c. cream at 6 a. m. The ratio for the twenty-four hours November 11-12 was 3.68. The excessive nitrogen excretion which was a prominent feature with William G. was absent here. The fall in both glycosuria and ratio during fasting is evident from Table 2.

Cyril K., the patient of Geyelin and DuBois, fasted five days without abatement of any of the diabetic symptoms, and with acidosis steadily increasing either because of the fast or in spite of it. Then, on account of dyspnea and drowsiness threatening coma, he was given low diet for a few days, consisting chiefly of protein, though containing also 53.3 gm. carbohydrate December 14 and 23.5 gm. December 15. The dextrose-nitrogen ratios for the next three days (December 15 and 17 inclusive) were 3.97, 4.01, and 3.87. The nitrogen loss at this period was greater than ever before described in uncomplicated diabetes. Beginning December 17, the condition gradually yielded to the second fast-treatment, as indicated by the fall of sugar, nitrogen, the ratio and the acidosis.

The case of Gephart, Aub and DuBois appeared at first to be of no extreme severity, and the urine was readily cleared up by fasting. Thereafter, in consequence of excessive protein-fat diet and the simultaneous development of an alveolar abscess, glycosuria suddenly appeared, and by the second day the 3.65 ratio was attained. The condition then yielded promptly to a repetition of fasting.

It is desirable here to discuss the dextrose-nitrogen ratio as respects (a) its occurrence in human diabetes, (b) its practical and (c) its theoretical significance.

(a) Lusk has insisted that trustworthy ratios are obtainable only when the diet contains no appreciable quantity of carbohydrate. The examples in the entire literature are very few, largely because the type of patients most likely to show the maximum ratio has so seldom been subjected to the conditions necessary to establish the ratio. Foster[28] says: "The diabetic patient is for several reasons an extremely difficult subject for these experiments. It is usually impossible to restrict him for a period of a week to a fat-protein diet." Benedict and Joslin[4] mention the danger of placing a patient with severe diabetes upon a strict protein-fat diet for several days. Joslin[5] also calls attention to possible errors due to excretion of retained carbohydrate unless ade-

28. Foster, N. B.: Diabetes Mellitus, Lippincott Co., Philadelphia and London, 1915, p. 30.

quate precautions are taken. The conditions involved in fasting differ in some respects from those of protein-fat diet. Though sometimes an existing ratio of 3.6 rapidly diminishes on fasting, and the glycosuria clears up, in other cases this ratio is clearly developed and persists for at least several days. Since the introduction of the fasting treatment, examples, mostly unpublished as yet, of such a ratio have been observed by several clinicians. It is probable that such observations will henceforth be made more frequently, not because the incidence of such "total" diabetes is increased by the fasting treatment, but because this method involves placing severely diabetic patients as a routine measure upon a program of complete carbohydrate abstinence for considerable periods, thus facilitating demonstration of the ratio with freedom from previous difficulties and errors. This is one of the features in which the new treatment has proved of service not merely for the practice, but also for the theory, of diabetes.

(b) Recent experience confirms the suggestion of Lusk[13] that the presence of the above-mentioned ratio need not be permanent or carry a rapidly fatal prognosis. In the patient as in the phlorhizinized animal, the relation between sugar and nitrogen in the urine under suitable conditions is an index of the deficiency of carbohydrate combustion, and the maximal ratio shows total absence of utilization of the sugar formed from protein. This ratio does not necessarily indicate the highest possible quantity of protein catabolism or sugar excretion. The nitrogen excretion of Gerald S. was never high. William G. showed markedly excessive protein destruction at first; later (January 15) the ratio was maximal, but the protein breakdown moderate. Cyril K., as above remarked, showed the most rapid nitrogen loss ever recorded in a case of diabetes, and this loss was still excessive on December 22-23, when the ratio had fallen to 1.12. Phlorhizin given to Gerald S. could not have increased the ratio but would perhaps have increased the quantities of sugar and nitrogen excreted.[29] The reason for the remarkable intensity of protein catabolism in some cases is not known. There is no justification for the term "toxic" applied by Magnus-Levy and others. So far as existing data permit judgment, the difference does not lie in acidosis, for the patients mentioned seemed about equally close to coma. The bodily strength and nutritive state may play a considerable part. For example, Cyril K. (Geyelin and DuBois), with recent acute diabetes, had the necessary strength and reserves for intense waste of sugar and nitrogen, like the typical experimental animal. Gerald S. was weak and emaciated. William G.

29. This remark applies to fasting. On liberal protein-fat diet Benedict and Lewis (The Influence of Induced Diabetes on Malignant Tumors, Proc. Soc. Exper. Biol. and Med., 1914, xi, 134), found the nitrogen excretion of human subjects not increased by "total" phlorhizination (personal communication).

was weaker in the second of the periods described than in the first, and weighed some 5 kg. less. But this may not be the whole explanation. A specific disorder affecting protein metabolism in some patients, as in totally depancreatized dogs, is not excluded. The possibility of very rapid changes in the ratio, as exhibited most strikingly by the patient of Gephart, Aub and DuBois, is one of the strongest evidences in favor of the functional element in human diabetes. Such sudden changes for the worse or for the better are scarcely to be expected in the case of purely organic lesions, and are contrary to the results in animals when the islands of Langerhans have been lost. Because of the generally more favorable outlook for functional as opposed to organic disturbances, the dextrose-nitrogen ratio therefore contributes something to the prognosis in human diabetes. For the very reason that the process is at least partly functional and under appropriate treatment may be temporary, the dextrose-nitrogen ratio fails to define the later prognosis in any individual case. Aside from the duration of the trouble and other fallible clinical indications, there is now no basis for predicting which patients are likely to recover tolerance quickly and in considerable degree, and which are likely to improve slowly and in slight measure. Experience to date indicates that cases of brief acute course, when checked by radical treatment, may show a correspondingly more rapid improvement as compared with the more protracted cases in patients of corresponding age and type. The occurrence of the dextrose-nitrogen ratio of the phlorhizinized dog in any human patient may be taken as a sign of the gravest immediate significance. The few known to have exhibited this ratio during fasting have died, except the patient of Geyelin and DuBois. The exception is believed to be due to the skilful alternation of fasting and protein feeding in this case, but further experience will be necessary for decision. It is at least established that careful treatment offers some hope even in cases of this type, and that with the worst of ratios and other symptoms an appreciable carbohydrate tolerance may subsequently be regained.

(c) The principal debate concerning the dextrose-nitrogen ratio has been not whether values as high as those mentioned occur in human patients, but whether any higher values ever occur. Animal experiments aiming to prove the formation of sugar from fat have all miscarried; but a few authors still hold that occasional cases of exceptionally severe human diabetes show dextrose-nitrogen ratios so high as to be explainable only by the formation of sugar from fat. Some of the cases above described are not lacking in severity, but rather give the impression of being more severe than those in the literature in which sugar was supposed to have been formed from fat; and neither on protein-fat diet nor on fasting were any ratios observed which could justify the assumption of sugar-formation from fat. It may be argued

that the negative evidence in the present cases cannot overthrow positive evidence in other cases, which though not more severe may have been of peculiar character. Alone, it could not do so. But the carbohydrate hunger of patients on old-fashioned protein-fat regimen caused numerous writers to compare them to drug addicts with respect to their ingenuity, pertinacity and also mendacity in obtaining forbidden food, even when supposedly isolated and watched; and experienced observers are aware that only special environment and special qualifications of the nurse in charge can guarantee against this source of error. As accuracy of investigation has increased, the number of reports of ratios indicating sugar formation from fat has diminished. Apparently no such ratio has ever been described in America; and the experience of the majority of clinics and laboratories elsewhere is similar. The justification for questioning the alleged findings in occasional cases at a few European clinics is found in the large number of accurate observers who see numerous diabetics of various grades of severity, but are still waiting to see any case showing the excessive ratios mentioned. The general agreement of negative evidence is believed now sufficient to set aside the principal support of the doctrine of sugar formation from fat, namely, the supposed occurrence of this process in diabetic patients.

3. *The Respiratory Quotient.*—In the cases mentioned, except that of Cyril K., the Lusk dextrose-nitrogen ratio was present only for brief periods. The objection might therefore be raised that these ratios were purely accidental, and partly accounted for by sweeping out of more or less carbohydrate previously retained as glycogen or sugar. Here the necessary proof is afforded by the respiratory quotients. In the case of Gerald S. it was impossible to determine accurately the dextrose-nitrogen ratio November 9, the day after a considerable amount of carbohydrate in the food, so it was assumed for purposes of calculation to be 1.5, a figure which gave theoretical results. On the second day of the fast, the dextrose-nitrogen ratio being 3.5 during the calorimeter period, the total quotient was 0.697 and the nonprotein quotient 0.7. On the sixth and eighth days of the fast the nonprotein quotients were 0.701 and 0.701 respectively. For William G. in the last two experiments (January 15 and 22), with dextrose-nitrogen ratios of 3.81 and 3.12 during the calorimeter periods, nonprotein quotients of 0.714 and 0.693 were found. The average nonprotein quotient on all these days was 0.703, as compared with the theoretical figure of 0.707 for fat. These and the similar quotients observed in Cyril K. serve to show that the dextrose-nitrogen ratios obtained under the above conditions were not accidental, but at the times when the Lusk ratio was present the diabetes was actually "total." These quotients also agree with the results of Benedict and Joslin and other exact work in fur-

nishing additional testimony against the formation of sugar from fat, thus fully confirming the evidence afforded by the dextrose-nitrogen ratio.

The tables also show that during the fasting treatment the power to oxidize carbohydrate gradually improved, as would be expected from the urinary findings. On fasting and on low diet thereafter the patients were able to derive an appreciable percentage of the energy requirement from this source. Joseph U. was able thus to derive 8 per cent. of his requirement. Gerald S., from a condition of total inability to oxidize sugar, apparently became able to derive 15 per cent. of his energy from it. William G. illustrated the opposite change produced by protein-fat overfeeding. January 11, on low diet, he was deriving 7 per cent. of his requirement from carbohydrate. The protein and fat were then increased, and by January 15 "total" diabetes was present.

Brief mention may also be made of the two exercise experiments with Gerald S. on December 2 and 4. The exercise performed in the calorimeter consisted in flexing and extending the forearms for ten minutes at the beginning of a period. The labor performed was sufficient to raise the heat production by 18 per cent. for the hour period, or by about 100 per cent. for the ten minutes of actual exercise. The respiratory quotient showed no change during this hour, remaining at 0.75; but in the next hour the total quotient was 0.779 and the nonprotein quotient 0.77, which figures are higher than the averages obtained in any of the experiments with this patient at rest. On December 4 a similar ten minutes of exercise was inserted at the beginning of the preliminary period, immediately after the calorimeter was sealed, and also at the beginning of the first and second hours thereafter. The quotient in the first hour was 0.778, corresponding to that on December 2; the quotient in the second hour was lost through accident. The experiments at least give no indication of a lowering of the quotient due to any hypothetical exhaustion of glycogen in a patient supposedly glycogen poor. This aspect is to be emphasized more than the slight rise of the quotient, which might have been accidental in the two experiments, though it may perhaps suggest a slight increase in carbohydrate utilization, possibly bearing some relation to the therapeutic benefits of exercise.[9]

The most surprising feature pertaining to the respiratory quotients consisted in some unexpectedly high values obtained, similar to those described by Joslin. For example, Gerald S. fasted eight days, November 11 to 19, then received a gradually increasing protein-fat diet, with from 750 to 1,000 gm. of thrice-boiled green vegetables daily. On the fifth day of this diet, November 23, the quotient indicated that he was deriving 2 per cent. of his calories from the combustion of carbohydrate. The subsequent experiments, up to December 7, gave quo-

tients indicating combustion of between 10 and 15 per cent. carbohydrate, with an average of 12 per cent. During this period the basal metabolism averaged 1,042 calories per twenty-four hours. If he were deriving 12 per cent. of his calories from carbohydrate, he must have metabolized an average of 31.3 gm. a day or a total of 438 gm. in the two weeks. According to the analyses of the thrice-boiled green vegetables, which were the only possible source of starches or sugars, he could not have received more than 2 or 3 gm. of carbohydrate a day. It is improbable that he could have maintained a store of 400 gm. of glycogen in his body under the circumstances. The blood sugar did not fall enough to suggest that more than a small fraction could have been derived from this source, and the recent work of Palmer[30] proves, as far as is possible with animal experiments, that the quantity of sugar present as such in the tissues is insignificant. The results after the ingestion of whisky are also hard to interpret. It is known that alcohol requires a moderate amount of time, sometimes several hours, for its complete combustion, but it is impossible to tell how much alcohol is metabolized each hour, since the nonprotein respiratory quotient will not solve a problem with three unknowns. Alcohol has a quotient of 0.667, but it may possibly cause vasomotor and respiratory changes leading to an elimination or retention of carbon dioxid with resulting false quotients. But its action in normal persons or animals is to depress the quotient; in all the extensive studies concerning the utilization and effects of alcohol, a rise of the quotient after its ingestion has never been reported. In the earlier whisky experiments with Gerald S., there was a sharp rise in the quotient after drinking, followed by a corresponding fall in the second hour, the highest non-protein quotients for single hours being 0.764 on November 18, and 0.773 and 0.782 on November 20. This was not seen in control experiments in which the patient drank the same amount of plain water at the same temperature, or went through the movements of drinking without swallowing any liquid. Mild exercise, as above stated, had no immediate effect on the quotient. Finally, on Nov. 25, the whisky was given in such a way that there was absolutely no exertion on the part of the subject, and although the rise of quotient in the first hour was absent, the marked drop in the second hour was present. In this last observation there was no apparent increase in the combustion of carbohydrates, but in the first three the average quotient of the hours after whisky was slightly higher than before. There was thus an apparent increase in the carbohydrate metabolism, which would be even higher than calculated if alcohol with its low quotient were oxidized, thus tending to lower the total quotient.

Joslin has suggested that combustion of retained acetone bodies, with their high quotients (beta-oxybutyric acid 0.89, diacetic acid 1.00),

30. Palmer, W. W.: In press.

may account for some rise in the quotients of these patients. The suggestion is supported by the observation that on fasting the ketonuria falls and the quotient rises. Also, if it should prove true that alcohol diminishes ketonuria, as claimed by authors[31] in the past, the rise of the quotient after ingestion of alcohol might correspond to an increased combustion of acetone bodies. The high quotients as described seem to be a regular or frequent phenomenon in patients with severe diabetes under the conditions described, and the possibilities may be discussed by comparison of the cases reported. The blood sugar, as stated, fell somewhat in the case of Gerald S., but rose during the development of the increased quotients in Geyelin and DuBois' patient (Cyril K.), and in the patient of Joslin.[19] The above calculation in the case of Gerald S. requires the equivalent of 400 gm. of glycogen to explain the quotients observed. No patient could possibly retain enough acetone bodies to correspond to the whole of this requirement. The high quotients have generally been observed when the glycosuria and ketonuria were diminishing either during or after fasting, or on ingestion of whisky. An exception is present in the case of Cyril K. when receiving protein diet on December 16-17. Here the ketonuria was higher than on any previous day, namely, 75 gm. reckoned as beta-oxybutyric acid. The carbon dioxid capacity of the blood plasma had fallen to its lowest point, namely, 19.6 (the normal figures being from 40 to 45). The dextrose-nitrogen ratio was at its highest point, namely, 4.01. Under these circumstances it is difficult to understand what kind of material could be burned to give the observed nonprotein respiratory quotient of 0.743. This single result may possibly be due to some accident connected with the circumstances of this particular case. On the other hand, it may possibly be of some significance in connection with the fact that, although all the laboratory tests aside from the respiratory quotient indicated that the patient was in no wise better and in some respects worse on December 16-17 than on December 9-10, yet it was evident clinically that his condition was much better on the latter date and the symptoms of intoxication greatly diminished. This patient was receiving alkali during this period, but Gerald S. and Joslin's patient received none; therefore the quotients can scarcely be due to dosage with bicarbonate. It is conceivable that high quotients in one part of the twenty-four hours might be compensated by low quotients in another part. No respiration experiments were performed at night, but it is scarcely probable that any marked difference existed between

31. Neubauer, O.: Ueber die Wirkung des Alkohols auf die Ausscheidung der Azetonkörper, München med. Wchnschr., 1906, liii, 791. Benedict, H., and Török, B.: Der Alkohol in der Ernährung der Zuckerkranken, Ztschr. f. klin. Med., 1906, lx, 328. Stäubli, C.: Beiträge zur Pathologie und Therapie des Diabetes mellitus, Deutsch. Arch. f. klin. Med., 1908, xciii, 107.

day and night. Such a difference would in itself constitute an abnormality, for the day and night quotients have never been known to vary to such an extent in previous experiments on normal persons and animals. It is noteworthy that while the average divergence between the methods of direct and indirect calorimetry in the present series was only 2.3 per cent., and the agreement was close in the first experiments with Gerald S., yet beginning with the eighth day of his fast, November 18, when the period of high quotients began, there appeared minus errors of the direct as compared with the indirect calorimetry sometimes as high as 21, 14 and 16 per cent. Such discrepancies might in part be explained if the quotients were due to combustion of some other material, perhaps acetone bodies, instead of carbohydrate as assumed, for then the reckoning of the indirect calorimetry would be considerably altered. On the other hand, the divergence may possibly have been due to technical error in the measurement of the average temperature of the body.

4. *The Total Metabolism.*—In regard to the general question of heat production the present series of experiments agrees with the work of previous authors in showing the basal metabolism per kilogram of body weight to be increased in severe diabetes. But as above mentioned, the principal need in connection with this vexed question has been a satisfactory standard of comparison between diabetic and nondiabetic subjects. The linear formula devised especially to throw light on this subject is believed to afford such a standard, and the conclusions in the present paper are drawn on the basis of this mode of calculation. The summary in Table 8 shows that the surface area of thin diabetics is not so much smaller than that of normal men as would be indicated by Meeh's formula, and consequently their metabolism is considerably lower when compared with the normal average according to the linear or height-weight formula than when Meeh's less accurate formula is used. The difference between the results as expressed in terms of the two formulas in the case of Gerald S. is from 8 to 13 per cent. With William G. it is from 11 to 18 per cent., with Joseph U., 10 per cent., with John O'C., from 11 to 12 per cent. These were all very thin diabetics, and the differences with less emaciated patients would be proportionately smaller. With patients stouter than the average the metabolism would be higher according to the linear formula than according to Meeh's, but patients with severe diabetes are seldom stout.

Among the patients described in the present paper, it was noted that Gerald S. entered the hospital in a weak and exhausted condition. His metabolism at this time, November 9, was 2 per cent. above the average normal by Meeh's formula, but 8 per cent. below the average normal by the linear formula. William G. had been subjected to

prolonged low diet. Starting at 26 per cent. below normal on January 11, when glycosuria was absent, his metabolism rose, on increased diet and the return of active diabetes, to 20 per cent. below normal on January 15 and to 11 per cent. below normal on January 22. On the other hand, in the patient of Geyelin and DuBois[26] (Cyril K.), the diabetes was recent and acute, and here the metabolism was above normal. The respiration experiment on December 15 was after food, therefore the metabolism of 15 per cent. above normal does not represent a true basal value. The highest basal metabolism actually demonstrated here was 3 per cent. above normal on December 18.

The patient Edward M. never showed the true ravenous hunger of diabetics, but had been a heavy eater all his life and could dispose of a large diet exceptionally well, with no increase of his slight dyspeptic complaints. During most of September, weighing 58 to 63 kg. and leading the inactive life of a ward patient, he had enjoyed a high diet, the maximum being during the period September 21 to 26, with from 6,100 to 6,300 calories daily, consisting chiefly of fat, of which there was nearly 600 gm. daily. Instead of steatorrhea, there were small constipated stools, showing exceptionally high utilization by analysis. As stated in his history, the diet had been moderate but adequate preceding the first calorimeter tests. The body weight was about 60 kg., as opposed to his original "normal" weight of about 80 kg. But he felt well and strong at this weight, and, correspondingly, the basal metabolism on October 30 was found entirely normal, 3 per cent. below the average. On October 31 the metabolism was measured two to five hours after drinking 97 gm. olive oil. Table 8 shows the resulting increase of metabolism and lowering of the respiratory quotient. On November 3 the diet contained 5,300 calories with 483 gm. fat, and on November 4, 5,268 calories with 482 gm. fat. On the morning of November 5 the patient entered the calorimeter after taking 44 gm. protein, 38 gm. carbohydrate and 204 gm. fat. The metabolism two to five hours afterward is shown by Table 8 to average 17 per cent. above normal. Accordingly, the specific dynamic action of food, especially of fat, did not differ noticeably from the normal as respects its promptness or intensity in this patient, and there was no indication of an abnormally high metabolism ("Luxuskonsumption") on the excessive diet. The result with this patient under the conditions does not warrant a positive conclusion concerning possibilities in more severe cases, especially at the height of the diabetic process.

Since the last important discussion of the total metabolism in diabetes by Benedict and Joslin there have been several changes in the general point of view of the metabolism of normal controls and of diabetics as the result of work presented in previous papers of this series. In the light of these it has seemed advisable to recalculate the

cases of severe diabetes reported in the literature, and discuss the question in its most recent aspects. As we have shown, it is advisable to abandon comparisons made on the basis of cubic centimeters of oxygen per kilogram and minute and use instead the calories per square meter per hour. Recent work on the metabolism at different ages has emphasized the fact, first brought out clearly by Magnus-Levy and Falk,[32] that metabolism changes with age. It must be remembered that a study of the surface area designed primarily to afford a basis of comparison between patients and normal controls has shown that Meeh's formula is not so accurate as the newly devised linear and height-weight formulas. Most important of all has been the study of a large number of controls by Benedict, by Means[32] and by the Russell Sage Institute staff, giving a normal basis of comparison which is not influenced by variations that might occur in small groups or by single investigators.

In Table 9 are given the results obtained in a large number of cases of severe diabetes. Since the height-weight formula was employed as a basis of comparison, the only cases that could be used were those where the height was given. This unfortunately has prevented the recalculation of the severe cases of Leo,[34] Nehring and Schmoll,[35] Rolly,[7] and some of the cases of Magnus-Levy[14] and Mohr.[36] The work of Leimdörfer[17] has not been recalculated, since the abnormally low quotients make this impossible, nor has the work of Grafe and Wolff,[37] where it is difficult to reconcile the high respiratory quotients and high dextrose-nitrogen ratios. As will be seen, the large majority of cases was furnished by the careful work of Benedict and Joslin. For purposes of comparison, columns have been added showing the duration of life after the period of experimentation, the level of the nitrogen metabolism, the degree of emaciation, and the estimated degree of acidosis. If we study first the column showing the percentage variation from the normal, it will be noted that out of twenty-six cases thirteen are within the normal range of plus or minus 10 per cent. from the average. There are nine patients with an increase

32. Magnus-Levy, A., and Falk, E.: Der Lungengaswechsel des Menschen in den verschiedenen Altersstufen, Arch. f. Physiol., 1899, Suppl., 314.

33. Means, J. H.: Basal Metabolism and Body Surface, Jour. Biol. Chem., 1915, xxi, 263.

34. Leo, H.: Ueber den respiratorischen Stoffwechsel bei Diabetes mellitus, Ztschr. f. klin. Med., 1891, xix, Suppl., 101.

35. Nehring, O., and Schmoll, E.: Ueber den Einfluss der Kohlehydrate auf den Gaswechsel des Diabetikers, Ztschr. f. klin. Med., 1897, xxxi, 59.

36. Mohr, L.: Untersuchungen über den Diabetes mellitus, Ztschr. exp. Path. u. Ther., 1907, iv, 910.

37. Grafe, E., and Wolf, G. L.: Beiträge zur Pathologie und Therapie der schwersten Diabetesfälle, Arch. f. klin. Med., 1912, cvii, 201.

of from 11 to 23 per cent. and these deserve special attention. Two of these, V. and Cyril K., were studied after food, and if the stimulus of the recent meal were removed they might have come within normal limits. One of the subjects, G., was under intense nervous excitement during the experiment, and another, I., with a pulse of 120, had been described the year before as very nervous. This leaves us five cases in which there was a moderate but distinct rise in the metabolism, namely, Herr Mo., Frau Schm., Frau St., H., and U. To these we should perhaps add Cyril K. at the time of his first experiment, when after a breakfast his metabolism was 15 per cent. above the normal basal. To offset these there are four patients whose metabolism ranged from 14 to 19 per cent. below the average. Three of these, N., P. and Q., were children, and it is quite possible that the normal stimulus of the growing organism was checked by the diabetes. The fourth subject, Wm. G., was extremely emaciated. If we take the algebraic mean of the 26, we find that the metabolism in severe diabetes averages 3.3 per cent. above the normal, a figure which might be increased to about 5 per cent. by taking into account the fact that the average for the 89 normal controls of Benedict is 2 per cent. lower than the Sage standards.

Benedict and Joslin[4] found that the average oxygen consumption of their diabetics per kilogram and minute was 15 to 20 per cent. above that of their twenty normal controls. Part of this difference was due to the fact that at that time few investigators realized the importance of the age factor. Part was due to the unusually low metabolism of the normal controls. In the twenty controls used by Benedict and Joslin for comparison with the diabetics, there are seven whose metabolism is 10 per cent. or more below the average normal described in the previous papers of this series. It so happens that these seven, A. F. G., T. M. C., Dr. P. R., Dr. S., H. F. T., E. P. C., Mrs. S. C., are used seventeen times in the total column of thirty-two, making the average of the column 8.6 per cent. below the standard. This is much greater than the divergence of —2 per cent. found in the total of eighty-nine normal controls. Their cases with severe diabetes, recalculated in terms of the height-weight formula, average only two per cent. above the Sage normal standard. It would appear that the metabolism of Benedict and Joslin's diabetic patients is within normal limits, while the large difference between their pathologic and normal cases is due chiefly to the low metabolism of the subjects selected for normal controls. It is quite possible that the low metabolism of these controls was due to the fact that they were poorly nourished and were selected because they resembled diabetics in this respect.

TABLE 9.—The Basal Metabolism of Patients with Severe
Surface Area as Estimated by

Investigator	Subject	Sex	Age, Yrs.	Calories per Sq. M. per Hr. Height-Weight Chart	Normal Standard Cal. per Sq. M. per Hr. for Same Age and Sex	Per Cent. Variation from Normal Standard	Respiratory Quotient, Average
Magnus-Levy	Herr Mo.	♂	43	46.9	39.7	-18	0.70
	Frau Schm.	♀	35	41.2	36.9	+11	0.72
Mohr	Frau St.	♀	52	40.5	32.7	+25	0.71
Benedict and Joslin	A	♂	50	36.6	35.2	+ 4	0.71
	B	♀	40	36.0	36.9	− 2	0.73
	C	♂	28	40.1	39.7	+ 1	0.70
	D	♂	39	36.9	39.7	− 7	0.74
	G	♂	35	45.1	39.7	+14	0.73
	H	♀	38	40.9	36.9	+11	0.77
	I	♂	25	45.2	39.7	+14	0.73
	J	♂	20	43.6	39.7	+10	0.76
	K	♂	46	39.1	39.7	− 2	0.72
	L	♂	23	43.5	39.7	+10	0.73
	N	♂	14	43.0	49.9	−14	0.74
	O	♀	16	37.9	39.0	− 3	0.72
	P	♂	15	39.7	49.0	−19	0.69
	Q	♂	14	42.2	49.9	−15	0.77
	R	♂	47	43.6	39.7	+10	0.72
	S	♂	37	34.2	35.2	− 3	0.73
	T	♂	44	39.6	39.7	0	0.73
	U	♀	37	42.4	36.9	+15	0.73
	V	♂	36	45.8	39.7	+15†	0.73
Geyelin and DuBois	Cyril K Dec. 15 & 16	♂	21	44.2	39.7	+11†	0.70
	Dec. 18	♂	21	40.8	39.7	+ 3	0.71
Authors	Gerald S. Nov. 9 & 12	♂	17	39.7	39.7§ (42.0*)	− 5 (−10*)	0.71
	William G. Jan. 15 to 22	♂	29	33.7	39.7	−15	0.70

* Using average normal for age of 17.
† Part of increase due to recent food.
§ Using average normal for ages 20 to 50.

DIABETES COMPARED WITH NORMAL STANDARDS ACCORDING TO THE THE "HEIGHT-WEIGHT" FORMULA

Time Before Death in Months		Urine N per Day, Gm.	Emaciation or Per Cent. of Loss from Greatest Weight	Degree of Acidosis	Remarks B = Beta-oxybutyric Acid per Day
Coma	2	.....	++	++?	
Coma	6	.....	++	++?	
.....		.....	.....	±	Moderately severe; Diac. 0 to -
			Per Ct.		
Tb.	20	6-14	10-18	+	NH_3N 3.3, Diac. +, Active Tb. in lungs
Coma	6-1	.....	9-18	- - -	Diac. ++++
Coma	2	13-22	14-24	+++	B 14 to 61; NH_3N 2.6 to 5.6
Coma	3	13	15	0:+	Diac. 0 to - - - -, urine alk. with 8 to 45 sod. bicarb.
Coma	15	17	+	+++	B 30, NH_3N 4.2, Diac. - - - -, intense nervous excitement during experiment
Coma	4	9-12	14	+	B 8 to 11, Diac. 0 to -
	15	14	30	±	B 4.8, NH_3N 2.2, pulse 120 nervous
	36	.....	15	±	Diac. + to ++, nervous temperament
Coma	16-4	16-20	20-24	0:++	B 30, Diac. 0 to - , NH_3N to 5.8
Alive		.....	20-16	±	Diac. 0 to sl. +
Coma	$1^1/_2$	5-10	9	+++	B 21 to 30, Alv. CO_2 Hald 10 to 8
Coma	3	8-11	14	+	B 12 to 14
Coma	1	5-18	20	+++	Diac. ++++, NH_3N 4.6 to 5
Coma	4	7-14	5	++	B 20 to 27, NH_3N 2.2 to 4.6, Alv CO_2 31 to 40
Tb.	10	13-16	17	++	B 42 to 70, NH_3N 5 to 6, somewhat nervous, moved considerably
Coma	5	7.3	18	+	Diac. ++, NH_3N 1.2
Coma	1	9-12	28	+++	B 40 to 60, NH_3N 4.6 to 7.2, Bon's
Coma	15-3	7-9.5	20	++	B. 18 to 22, NH_3N 3.6 to 4
Pneu.	11	.....	6	0	Diac. 0. After light breakfast
Alive		36-37	27	+++	B 71 to 75, blood CO_2 46 to 50 After large breakfast
Alive		29	27	+++	B 58, blood CO_2 35, second fast day
Coma	4	11-15	31	++	B 3 to 14, NH_3N 3.4 to 4.7
Coma Tb.	2	14-20	42	+	Diac. - -, NH_3N 3.4, B 0.1 to 1.3

The profound effect of confinement and undernourishment on heat production has never received the attention it deserves. The reduction of metabolism in fasting has been shown in several experiments, the best being the recent work of Benedict,[20] whose subject L. fasted thirty-one days. On the first day of the fast he produced 40.3 calories per square meter per hour as measured while awake in the morning and as calculated by the height-weight chart. This figure is 1.5 per cent. above the normal average for similar conditions. On the tenth day of the fast the metabolism calculated in the same way was 16 per cent. below the average, and it remained between 18 and 22 per cent. below during the rest of the fast. A similar or even greater lowering of metabolism results from prolonged undernutrition. The figures of Svenson and others[38] for emaciated typhoid convalescents when compared with the normal standard indicate a metabolism considerably below normal in some instances. By similar calculation, the results of Magnus-Levy[39] with a neurasthenic youth who partially starved himself for a long period, are as follows:

TABLE 10.—METABOLISM EXPERIMENT ON MAGNUS-LEVY'S PATIENT *

Period	Date	Condition	Calories per Sq. M. per Hour Height-Weight Formula	Weight, Kg.	Relationship of Metabolism to Average Normal 39.7
I	Nov. 16 to 21.....	Very low diet.....	26.6	36.2	—33%
II	Nov. 23 to Dec. 9.....	Liberal diet.....	33.0	38.0	—17%
III	Jan. 26 to March 6.....	Fever from Tb.	43.4	48.4	+ 9%
IV	March 13 to May 8.....	Normal again.....	40.5	52.2	+ 2%

* Age 19, height 160 cm.

These figures are comparable to those shown in the present series of diabetic patients after treatment. The degree of elevation of metabolism due to the active diabetic process should be judged by comparison of such patients with equally emaciated and cachectic nondiabetics. It is also now possible to compare the same patient at times when active diabetes is present or absent, while the body weight and surface remain the same. Thus Gerald S., with intense diabetes, on November 9 had a basal metabolism 8 per cent. below normal. His fast ended November 18, and from then until December 7 he received a diet such that his

38. Recalculated in terms of surface area according to Meeh's formula, by Coleman and Du Bois. The Influence of the High Calory Diet on the Respiratory Exchanges in Typhoid Fever, THE ARCHIVES INT. MED., 1914, xiv, 168 (Fig. 4).

39. Magnus-Levy, A.: Der Einfluss von Krankheiten auf den Energiehaushalt in Ruhezustand, Ztschr. f. klin. Med., 1906, lx, 177.

weight on the latter date was practically identical with that on November 9; but the basal metabolism on December 7 was 22 per cent. below normal at a time when the urine was free from sugar. William G. weighed 43.2 kg. on December 11. In consequence of feeding high-caloric diet, the weight fell to 42 kg. by December 22, while the metabolism rose from 26 per cent. below normal on December 11 to 11 per cent. below normal on December 22. If we study Table 9 it is apparent that most of the diabetics with marked emaciation have a diminution in metabolism. In the children with diabetes and low metabolism the percentage loss from the greatest weight is small, but with a child that is growing taller even a stationary weight indicates emaciation. If "normal" adults and children were as emaciated as the diabetics, they would undoubtedly show a marked diminution in heat production.

Benedict and Joslin have ascribed an increase in diabetes to acidosis. This is usually associated with an increased protein metabolism, and it is often difficult to separate the two factors. It has long been known that increased protein metabolism causes an increased heat production. If we turn to Table 9 we can compare the increased metabolism with the degree of acidosis. There were nine patients whose metabolism was 11 to 23 per cent. above the normal. Of these two showed marked acidosis, namely, Cyril K. and the nervous patient G. Three others, Herr Mo., Frau Schm. and U., had severe acidosis. Patient H. had moderate acidosis, while the others, I. and V., had little or no acidosis, and the patient Frau St., with the highest metabolism of all, had very slight acidosis. In contrast to this, eight patients with severe or very severe acidosis showed a normal or decreased metabolism. These are B., C., N., P., Q., T., Cyril K. (December 18), and Gerald S.

Authors have erroneously attempted a direct comparison between dogs depancreatized or phlorhizinized at the height of their strength, and human patients who reach the stage of severe diabetes, generally after months of a slow cachexia. Accurate comparison demands equally acute human diabetes, or else the use of dogs with chronic diabetes or prolonged cachexia. The excessive nitrogen excretion of William G. and especially of Cyril K. (Geyelin and DuBois) is well comparable to that of the totally depancreatized dog, and in the latter the total metabolism was actually above normal in spite of four weeks of rapid wasting followed by five days of complete fasting. The alleged difference as respects increase of metabolism can therefore no longer stand as a distinction between clinical and experimental diabetes.

Theoretically it is to be expected that the metabolism will rise with the increase of the protein metabolism which accompanies the noncombustion of sugar derived from protein in the diabetic condition. Since the specific dynamic action is less in human beings than in dogs, it may

well be that the stimulus of an increased protein metabolism is relatively less pronounced in human than in experimental canine diabetes.

Recapitulating, one may state that the linear formula furnishes a more accurate standard of comparison than was previously available. According to calculation by this formula, an increase above the true normal metabolism is not demonstrable in the majority of patients with severe diabetes. Nevertheless, the diabetic process may be associated with a relative elevation of metabolism. In occasional instances the metabolism may actually exceed the average normal level of metabolism. In all cases the true increase appears only when one takes into consideration other factors incidentally present, some of them tending strongly to depress metabolism. For example, the percentage of increase may be fully as great as claimed by Benedict and Joslin, if the metabolism of diabetics is compared with that of other equally undernourished subjects, or if the same patient is compared at different times when active diabetes is present or absent. In practical application, the results indicate that diabetics generally have no higher food requirement than normal, and on account of undernutrition and lessened muscular activity will tend to maintain equilibrium on a smaller number of utilizable calories than normal persons. Because the diabetic is less active, as pointed out by Magnus-Levy, his actual consumption of energy as compared with normal controls is likely to be less. After treatment by fasting, even though the patient is gaining steadily in strength and well-being, a low level of metabolism has been observed, the lowest 36 per cent. below normal, and this indicates that a low diet will suffice for maintenance under these conditions.

SUMMARY AND CONCLUSIONS

1. Three patients with severe diabetes and three with moderate or mild diabetes have been studied in the respiration calorimeter. The effects of the oatmeal treatment and the fasting treatment have been followed in detail.

2. No special influence of oatmeal in diabetes or special readiness of oxidation of this form of carbohydrate was demonstrable in these experiments. The respiratory exchange fails to account for all the carbohydrate that disappears. The behavior of the respiratory quotient showed no important difference on the first day and on the third day of the oatmeal treatment.

3. The occurrence of "total" diabetes in human patients, with dextrose-nitrogen ratios approximating 3.65 to 1 and corresponding respiratory quotients, is here shown. Notwithstanding the extreme severity, neither the sugar excretion nor the gaseous exchange gives ground for assuming the formation of sugar from fat in any instance.

4. Even in the severest type of diabetes the active symptoms may

be eliminated completely by prolonged fasting. The observations in the respiration calorimeter prove that patients as a result of the fasting acquire the power of oxidizing sugar derived first from their own body protein and later from the protein and carbohydrate of a carefully regulated diet.

5. The respiratory quotients during fasting and after the glycosuria had ceased were in some such instances higher than can be easily explained by the oxidation of the materials supposedly available. Also the ingestion of alcohol was sometimes followed by respiratory quotients higher than would theoretically be expected. The data will be analyzed in a subsequent paper.

6. The specific dynamic action of food, especially fat, was apparently normal in a patient with moderately severe diabetes.

7. The results of two respiration experiments in a severely diabetic patient have shown that mild exercise slightly raises the quotient, and this suggests the possibility that exercise may improve carbohydrate utilization. Generalizations or positive conclusions from these experiments are not attempted.

8. According to comparisons of the surface area as calculated by the linear formula, increase of the basal metabolism above the true normal level in severe diabetes is generally absent or slight. The metabolism was shown to fall markedly during fasting, to 20 per cent. below normal. The level of metabolism in diabetes is the resultant of a number of forces; for example, increased destruction of protein and perhaps other processes tending to increase metabolism, and undernutrition, muscular relaxation (as in prolonged confinement in bed) and other possible conditions tending to diminish metabolism. According as one or the other of these groups of forces predominate, a higher or lower metabolism may be expected in any individual case of diabetes.

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